



## PATHOGENESIS OF INTERMITTENT EXOPHTHALMOS

FRANK B WALSH, M.D., AND WALTER E DANDY, M.D.  
BALTIMORE

Intermittent exophthalmos is a rare, but striking and unmistakable, syndrome. It is characterized by pronounced and rapid—almost instantaneous—protrusion of one eye when venous stasis is induced by bending the head forward, by lowering the head, by turning the head forcibly, by hyperextension of the neck, by coughing, by forced expiration, with or without compression of the nostrils, and by pressure on the jugular veins. The ocular protrusion disappears immediately when the head is erect and when artificially induced venous congestion is relieved.

Usually, but not invariably, there is enophthalmos when venous congestion does not obtain. There may or apparently may not (to judge from cases reported in the literature) be pulsation of the eyeball. Vision may or may not be affected. The condition is progressive and may be productive of unbearable pain and troublesome diplopia. The appearance is unsightly, but life is not at stake.

The case here reported—the only one we have seen—is presented because the pathologic features were disclosed at operation. Most previous reports of cases are mainly clinical presentations, and the clinical study is not followed by detection of the underlying lesion. Orbital operations have been performed in a few cases, and venous beds have been described in the orbit. These may or may not represent the whole pathologic picture. No postmortem examinations have been made.

### REPORT OF A CASE

A white girl aged 18 was referred by Dr. Milton Little, of Hartford, Conn., with the complaint of bulging of the left eye induced by posture and associated with pain in the head.

The family and past histories were without significance.

*Present Illness*—From the age of 10 years the patient had known that her left eye was sometimes more prominent and at other times less prominent than her right eye. When she sat erect or stood, the left eye became sunken. When she lay down, it bulged. When

she became excited, it protruded. For six months, every morning on awakening, there had been a throbbing pain in the eye, which disappeared soon after she got up. The pain disappeared after rest in bed for a week, but on resumption of her usual activities it soon returned. For a week there had been severe pain in the left eye and the left temple. The throbs were noted to occur at the same rate as the heart beat. From the age of 10 years there had been occasional periods when diplopia was present, but strabismus or ptosis had not been observed.

*Examination*—When the patient stood, there was striking enophthalmos. Immediately after she lay down, the eye commenced to protrude, and pronounced exophthalmos persisted throughout the recumbent period. Moreover, the eyeball pulsated, this was visible and palpable. When she leaned forward (head down) the exophthalmos became extreme. This was also true when the jugular veins were compressed or when she blew her nose. The exophthalmos was also increased when the common carotid artery was compressed (because the internal jugular vein was then also compressed), but the pulsation ceased. There was no audible bruit.

There was weakness of the left external and inferior rectus muscles and absence of ptosis when the patient was sitting erect. When the eye was protruded as a result of change of position of the head, ptosis appeared. Measurements were made with the Hertel exophthalmometer. There was enophthalmos of 3 mm (fig 1 A) when the head was erect (in the sitting or standing position the measurement for the right eye was 15 mm and for the left eye 12 mm). There was exophthalmos of the left eye 6 mm when she was lying recumbent (fig 1 B), 11 mm when the head was tilted forward or the jugular vein was compressed (fig 1 C), 18 mm when expiration was forced and the nostrils were compressed (patient standing, fig 1 D), 5 mm when the head was turned forcibly to the left, and 3 mm when it was turned to the right. Visual acuity was 20/15 in the right eye and 20/30 in the left eye (with the patient sitting upright). The left pupil dilated slightly when the eyeball protruded. The eyegrounds were normal except for slight overfilling of the retinal veins of the left eye when that eye was maximally protruded.

Roentgenograms showed thickening of the superior margin of the left orbit, which was increased in density, as was the left wing of the sphenoid. The sphenoid fissure was widened (fig 2). A small, diffuse area of calcification was visible in the outer orbit (fig 2).

*Diagnosis*—1. The quick protrusion and sinking of the eyeball with the postural changes, and the rapid protrusion induced by coughing, sneezing and jugular compression could only mean filling of a large venous bed.

From the Johns Hopkins Hospital and University



2 The pulsation of the eyeball indicated an arterial component. The lesion, therefore, had to be an arteriovenous aneurysm.

3 The absence of a murmur indicated that the communication between arteries and veins was through vascular "coils," and not through a fistula.

4 The enophthalmos (with the patient sitting or standing) was thought to be due to atrophy of the orbital fat from long-continued pressure.

which the brain was free of attachment to the dura. The cerebral vessels were unaffected and of normal size. In the region of the sphenoid fissure and the anterior part of the middle fossa was a mass of coiled vessels (fig 3), this overflowed the sphenoid wing and extended a short distance over the orbital plate (about 1 cm) as a thin, pink film (of arterial blood), which blanched with slight pressure. The mass was intimately grown into, and was inseparable from, the dura and was



Fig 1—*A*, patient in the erect position, showing difference in the palpebral fissures. There is pronounced enophthalmos on the left side. *B*, degree of exophthalmos when the patient was recumbent. *C*, exophthalmos and downward protrusion of the eyeball from pressure on the jugular vein. *D*, exophthalmos induced by forced expiration when the nose was closed.

5 The most puzzling point was the absence of exophthalmos when the patient was erect. Coiled vessels could be expected to produce a space-occupying mass in the orbit. The explanation of this was obtained at operation. The coils making a space-occupying mass were in the cranial chamber, and not in the orbit.

*Operation (WED)*—On July 24, 1943, a fronto-temporal approach to the cranial chamber was made—a typical hypophysial approach. When the dura was turned back, a finger-like projection of vascular coils was observed extending from the region of the pterion backward and mesially, and finally paralleling the sylvian vein. A few minor vascular attachments to the brain were thrombosed with the electrocautery, after

made up of intertwining coils of vessels, easily compressible, like a sponge, and immediately returning to the original size when pressure was released. The vascular mass was repeatedly attacked by the electrocautery, and the volume gradually shrank until the scar was flush with the sphenoid fissure.

From time to time the cautery cut through the vessels, and brisk arterial bleeding occurred. The bleeding areas were covered with pieces of muscle, and the coagulation was carried out through them. The sphenoid fissure was greatly widened and filled with the vascular coils, but no attempt was made to carry the cauterization forward into the orbit, there being no reason to believe that a mass was located therein. Be-

cause of diffuse dural bleeding, the middle meningeal artery was isolated and coagulated at the foramen spinosum. It was our impression that the arterial component of the arteriovenous aneurysm arose from this vessel because of its intimate relation to the coiled mass and because no other large artery was nearby. The intracranial division of the internal carotid artery was distant and was entirely normal. The optic nerve was in full view, was not implicated and was not injured at any time. The aneurysmal mass completely covered the dura over the gasserian ganglion and the cavernous sinus. It could not be determined whether or not there were communications with the latter. That there were no communications with the internal carotid artery in the cavernous sinus cannot be stated dogmatically, but

or consensually to stimulation with light. Three months later the intermittent exophthalmos remained cured, but the extraocular paralyses persisted in part. The pupil exhibited a consensual reaction. There was enophthalmos of 3 mm. The upper lid could be elevated incompletely, and internal and downward rotation of the eyeball had improved to about half-normal. The price of a cure was therefore high, but the patient is happy over the end result. We have wondered whether it would have been practical and preferable to have attempted ligation of the orbital veins in the orbit (through the same transcranial approach) and to have left the aneurysm untouched. The practicability of this procedure is uncertain, but even if the operation had

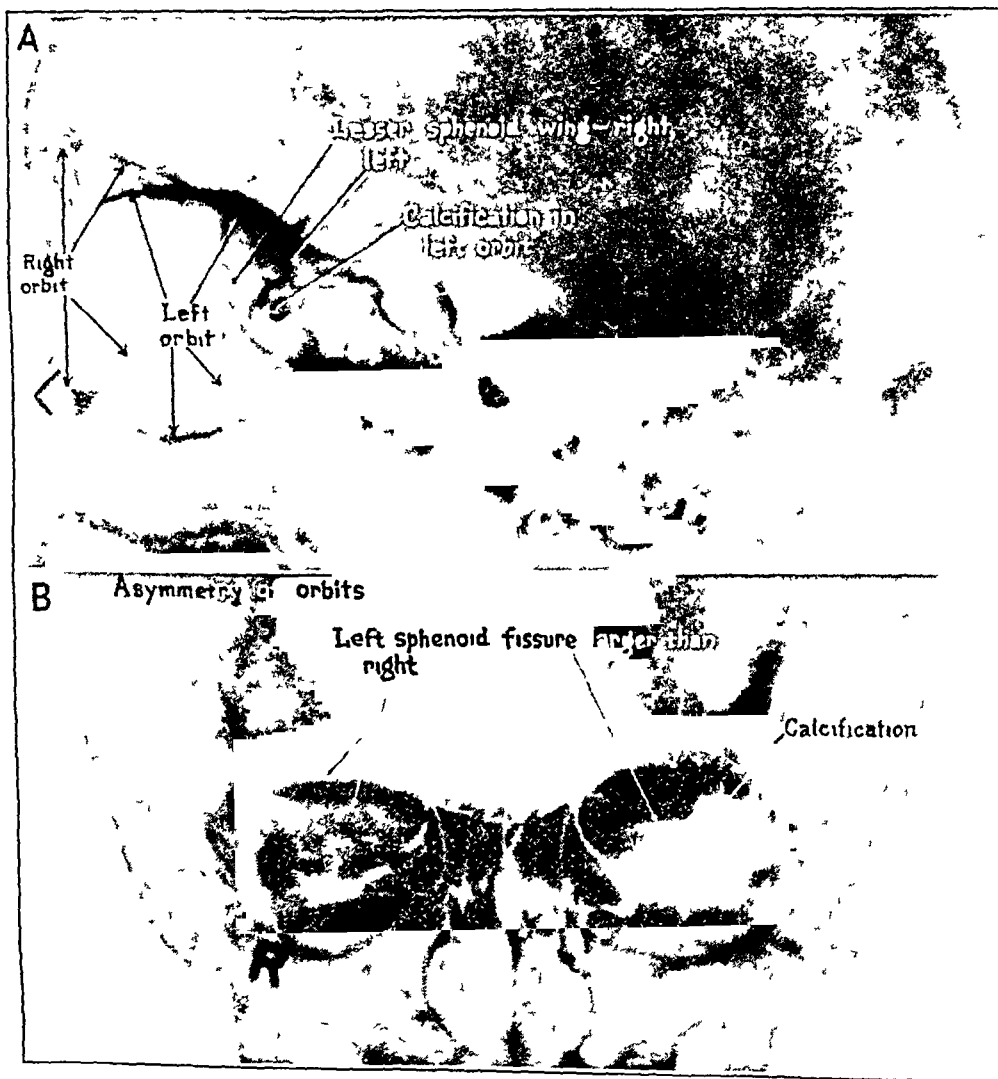


Fig 2—Retouched roentgenograms of the orbit, showing area of calcification and widening of the left sphenoid fissure

this could be possible only through an anomalous branch. It was realized throughout the operation that the nerves to the extraocular muscles lying in the cavernous sinus and the sphenoid fissure were passing through the vascular mass that was being coagulated, and that their injury, or even destruction, was a distinct possibility. However, the cure of the aneurysm was thought to be advisable in view of the progressively increasing pain.

*Postoperative Course*—Immediately after operation the eyeball was free of all the intermittent changes that previously obtained with posture, blowing the nose, jugular compression, etc. However, vision was entirely lost in the left eye, and all the extraocular muscles were paralyzed. The pupil did not respond directly

been successful, the pulsation of the eyeball would have persisted.

*NOTE*—The patient was seen again ten months after discharge from the hospital. There had been no discomfort except on one occasion, three weeks before reexamination, when she had a severe pain in the head. She stated that at this time there was some protrusion of the left eye.

Examination revealed incomplete ptosis and inward deviation of the eye of about 30 degrees. She was unable to elevate the left eye but could lower it 20 to 30 degrees. The eye was blind and the nerve atrophic. There was enophthalmos of the left eye, which was not influenced by such factors as position and pressure on the jugular vein.

SYMPTOMATOLOGY AND BRIEF REVIEW  
OF LITERATURE

Intermittent exophthalmos has been recognized as a clinical entity since 1805 when it was first described in an infant. In a classic paper, Birch-Hirschfeld reviewed the literature up to 1906 and presented observations of prime importance concerning not only the intermittent exophthalmos but the anteroposterior position of the normal eye in relation to various positions of the head. He described the syndrome in a physician Dr Minor, who also wrote regarding it. Wissmann and Schulz (1922) added a single

tor (1939), Giqueaux (1942), Poole (1942), Dunphy (1942) and Rones (1942). The cases reported by the two last-named authors were mentioned in the discussion on Poole's paper. Rychener (1942) and Ellett (1940) made subsequent reports on Chapman's case. These, with our case, bring the total number of cases to 111.

From the clinical viewpoint little has been added since Birch-Hirschfeld's comprehensive review.

*Occurrence*—As the foregoing figures indicate true intermittent exophthalmos is rare. Birch-Hirschfeld saw a single case among

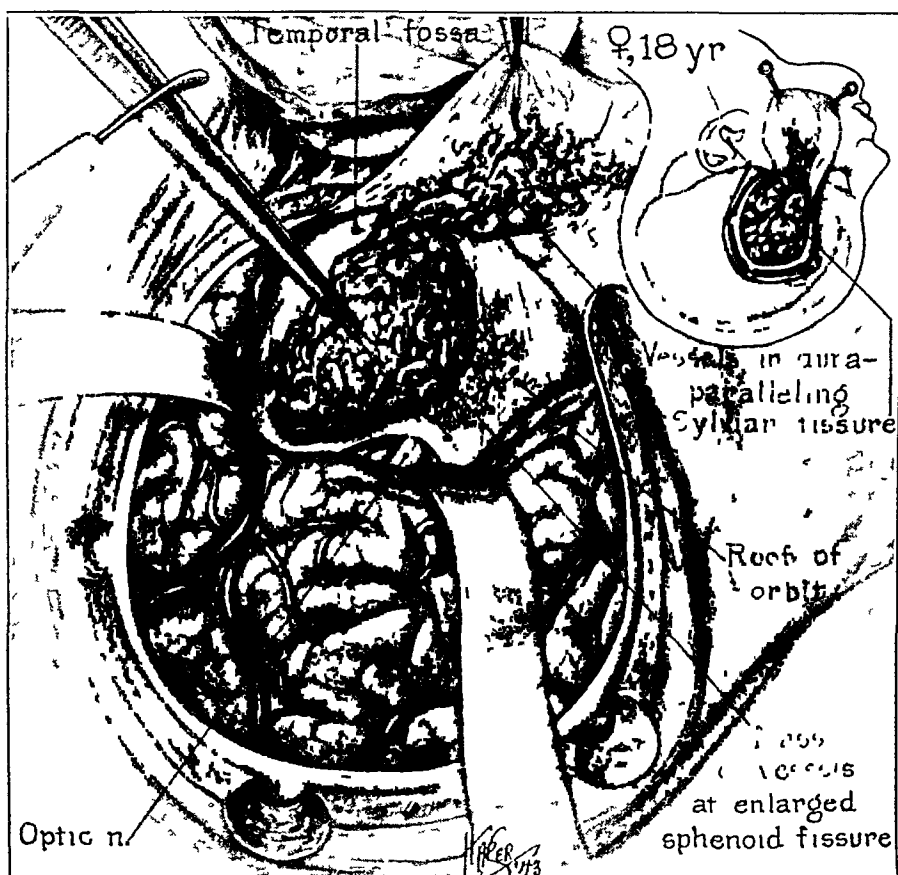


Fig 3—Coil of vessels forming an arteriovenous aneurysm which filled the floor of the middle fossa and overflowed around the sphenoid wing into the dura of the anterior fossa. These vessels contained arterial blood and pulsated.

case and collected the cases appearing between 1906 and 1922, a total of 74. Kraupa and Mendl (1936) described a case and brought the number reported in the literature to 96 cases. They rejected 2 cases included by Wissmann and Schulz.

The following reports of cases of intermittent exophthalmos have been found since Kraupa and Mendl's publication, and the list also includes 2 cases not mentioned by them: Bartok (1931), Chapman (1931), de-Petri (1935), Marchesini (1935), Hippert (1936), Muirhead (1936), Lipovich (1936), Petrov (1939), Spek-

tor (1939), Giqueaux (1942), Poole (1942), Dunphy (1942) and Rones (1942). The cases reported by the two last-named authors were mentioned in the discussion on Poole's paper. Rychener (1942) and Ellett (1940) made subsequent reports on Chapman's case. These, with our case, bring the total number of cases to 111. From the clinical viewpoint little has been added since Birch-Hirschfeld's comprehensive review.

*Sex*—Possibly more men than women are victims of this condition. Birch-Hirschfeld's series contained 35 men and 15 women. In

Kraupa and Mendl's series 10 patients were males and 8 females

*Trauma*—Trauma has been suggested as a factor in the development of intermittent exophthalmos, but it is difficult to believe it can play more than a precipitating role. The patient described by Rumjanzewa was first observed to exhibit the syndrome during childbirth.

*Age of Onset*—Since persons with intermittent exophthalmos may be wholly unaware of its existence until it has been pointed out to them, it is impossible to obtain accurate information regarding the age of onset. The condition has been seen in infants, and it has been observed for the first time during the sixth decade of life (Birch-Hirschfeld). Sattler expressed the opinion that it occurred in young persons almost, or quite, exclusively, but there is ample evidence that this concept is erroneous. Birch-Hirschfeld found records of 6 cases occurring in the first decade of life, 7 in the second, 8 in the third, 1 in the fourth, 2 in the fifth and 1 in the sixth. Of cases reported since 1935, 3 have occurred in the second decade of life, 4 in the third, 5 in the fourth and 2 in the fifth.

*Unilaterality*—In all reported cases the condition has been unilateral. Poole commented that the left eye is involved ten times as often as the right. This high ratio is not upheld by Birch-Hirschfeld's compilations, although he stated that the left eye was affected more often than the right. Kraupa and Mendl found the right eye affected in 10 cases and the left eye in 8 cases. In the 13 cases described since 1935, the left eye was always affected. Excellent accounts of intermittent exophthalmos of the right eye have been given by Byers and Rumjanzewa.

It is natural that attempts have been made to explain the predominance of involvement of the left eye. Reese suggested that the jugular foramen on the left side is frequently smaller than that on the right, but this structure is remote from the lesion producing the venous changes and can have no bearing on its causation. There is no apparent reason that a congenital lesion, such as that causing this condition, should favor one side.

*The Exophthalmos—Its Direction and Degree*—The complete syndrome of alternating exophthalmos and enophthalmos usually develops gradually and progressively. Radswitzki described a case of exophthalmos which occurred only as a result of severe coughing or vomiting up to the age of 14 years, but thereafter a change in position of the head, holding the breath, etc., was sufficient to induce the condition, which

rapidly disappeared when the head resumed the erect position. Mulder described the case of a man who until the age of 12 years exhibited intermittent exophthalmos only when he wore a tight collar but later presented the complete syndrome. Mention has already been made of Rumjanzewa's case, in which the anomaly developed during the strains of childbirth.

The eye may be protruded either directly forward or downward and outward. In a majority of reported cases mention is made only of direct protrusion. According to Birch-Hirschfeld, the superior ophthalmic vein is usually larger than the inferior ophthalmic and, consequently, the eye is usually pushed downward and outward, as well as forward. The position of the eyeball is doubtless dependent on the symmetry or asymmetry of the venous bed in the orbit.

Narrowing of the palpebral fissure during the episodes of exophthalmos was observed in Poole's and Rumjanzewa's cases and in our case. During the stage of enophthalmos the palpebral fissures on the two sides were quite, or almost equal in width. Probably Dunphy's suggestion that during exophthalmos there may be voluntary or reflex closure of the lids as a protective measure is correct.

The amount of proptosis has been noted to vary within wide limits in different cases. Sattler and de Vincentis observed 25 and 29 mm respectively in their cases when the head was bent forward. In our case, 18 mm of relative exophthalmos was observed when the patient exhaled forcibly with the nostrils compressed, but this did not represent what could have been obtained, since it was thought unwise to attain the maximum. It may be remarked that measurements of exophthalmos as usually made are only approximate, special photographic apparatus, such as that described by Birch-Hirschfeld, is necessary for accuracy.

The time required for proptosis to begin is not stated in most reported cases. Birch-Hirschfeld observed a latent period of five seconds, followed by protrusion of the eye, which reached almost its maximum in thirty seconds and its full maximum in another fifteen seconds. His patients had the head bent forward. He commented that the latent period had been stated as being from one to five minutes but that it rarely, if ever, is as long.

*Factors Influencing Exophthalmos*—Often, as in our case, the condition has first been observed by a friend. Birch-Hirschfeld observed protrusion of the normal eye when the head was bent forward. This, of course, is due to gravity and is intensified when an abnormal venous bed exists.

Proptosis can be produced in most instances by pressure over the jugular vein on the side of the intermittent exophthalmos. In our case this produced about as much proptosis as did bending the head forward. Occasionally, as in Lindenmeyer's case, pressure over the contralateral vein produced proptosis when similar pressure over the homolateral jugular vein failed to do so. In such instances, either there is great congenital narrowing or absence of the homolateral jugular vein, or it has become thrombosed.

The position of the head in lateral rotation has been found to influence the position of the eye, owing to a degree of jugular constriction. Mann observed that rotation of the head to the right produced maximal venous drainage through the left jugular vein, and conversely, rotation of the head to the left produced maximal venous drainage through the right jugular vein. In our case forcible turning of the head produced exophthalmos of the affected eye, which was more pronounced when the head was turned to the left. In Poole's photographs the effect is most striking.

Birch-Hirschfeld surmised that any obstruction to the anterior venous pathways outside the orbit resulted in additional pressure in the ophthalmic veins, and, to prove it, he devised an ingenious experiment by which the extra-orbital veins were compressed. This, however, could have no bearing on the intermittency of the exophthalmos. Krauss assumed that large congenital varicosities in the orbit might cause intermittent exophthalmos. He also assumed that an obstruction to the drainage of orbital blood, either anteriorly, as suggested by Birch-Hirschfeld, or posteriorly, could produce intermittent exophthalmos. Both these observers commented on the narrowness of the ophthalmic vein just before it enters the cavernous sinus, and Krauss remarked on there being a pronounced constriction of the superior ophthalmic vein where it lies close to the tendon of the superior oblique muscle. However, an obstruction to the veins is the one thing that cannot explain this condition, the prompt appearance of proptosis with jugular compression means that there is no obstruction in the venous channels. All textbooks are in agreement that there are no valves along the ophthalmic vein. There could not, of course, be any effective valves in intermittent exophthalmos because pressure on the jugular veins immediately produces the ocular protrusion.

*Enophthalmos*—Enophthalmos is not essential to the diagnosis, but it is usually present. It can only be due to absorption of orbital fat from pressure of the vascular bed (probably venous) in the orbit. Enophthalmos, when

present, is apparent only when the head is in the erect position.

*Lids, Temporal Region and Face*—It might well be expected that there would be some engorgement, or at least prominence, of the veins of the eyelids, temple and face on the side of the anomaly since they are in communication with the orbital veins. However, this is only occasionally observed and was not present in our case. Some swelling of the lids may be observed when the eye is proptosed. The temporal region was engorged during proptosis in Marchesini's case, and the homolateral side of the face was swollen in Petrov's case. In Rumjanzewa's case there was flushing of the side of the face when the eye was protruded.

In no instance so far as we are aware, has there been great dilatation of veins over the face and lids or over the scalp as is so commonly observed in cases of carotid-cavernous fistula and pronounced cirroid aneurysm.

*Facial Asymmetry*—In several instances retardation of growth of the homolateral side of the face has been described, but Birch-Hirschfeld concluded that this was not of particular significance because of the relative frequency of asymmetry of the face in otherwise normal persons. There can be no local reason for asymmetry of the face.

*The Affected Eye*—It is obvious from consideration of reported cases that the involved eye in a great majority of instances remains normal. When the eye is proptosed and remains so for a considerable time, there may be congestion of the bulbar conjunctiva. In a relatively small number of the reported cases some degree of optic nerve atrophy (14 per cent, Birch-Hirschfeld) has been present. In our case vision was slightly reduced—20/30. Birch-Hirschfeld assumed that optic nerve atrophy was due to retrobulbar hemorrhage, which is said to be, and doubtless is, an occasional complication. However, a more reasonable assumption in a majority of such cases would appear to be long-sustained direct pressure of the mass on the optic nerve.

Visual acuity may be lowered materially during the exophthalmic phase. Extreme overfilling of the retinal veins has been noted during the period of exophthalmos, and they may pulsate, but the fundus remains otherwise unchanged. Diplopia, present occasionally in our case, is not usually mentioned. Usually there is no limitation of ocular movements. The pupil remains unchanged in many cases, but pupillary dilation during exophthalmos has been described by several observers listed by Birch-Hirschfeld and was present in our case. Rumjanzewa described

narrowing of the pupil during periods of exophthalmos in her case

*Pulsation of the Eyeball*—According to Birch-Hirschfeld, this symptom is rarely present in cases of intermittent exophthalmos. Mention of it was made in only 7 of 74 cases included in his study and in that of Wissmann and Schulz. The symptom was present in our case and was most pronounced during maximum exophthalmos. It is entirely possible that the pulsation was overlooked in some of the reported cases in which it was not mentioned. However, in many cases special mention has been made of the absence of pulsation, and there can hardly be a doubt that it is not always present. In only 1 instance has a subjective murmur or objective bruit been noted. In Delord and Viallefont's case a blowing sound was heard on auscultation. Poole's patient described roaring and tinnitus. Neither was present in our case despite the known arteriovenous communication.

*Other Symptoms*—In many cases the condition is asymptomatic, but pain may be the only symptom, and it may become steadily more severe. Since pain is associated with protrusion of the eye, it may be present most of the time. A sensation of fullness in the side of the face is frequently noted. In Poole's case the pain became so severe that the patient could not continue his work. Often there is complaint of dizziness and vertigo, usually not severe and occurring only during periods of exophthalmos. Birch-Hirschfeld, in a short discussion (1930), suggested that intracranial varices possibly account for these symptoms. Hippert expressed the opinion that venous anomalies influenced the vestibular apparatus in his case.

*Roentgenograms*—Roentgenographic evidence has usually been reported as negative. Hippert noted a single small calcification in the sphenoid fissure, but there was a similar one on the other side. Kiaupa and Mendl reported small calcifications, which they termed phleboliths, in 2 cases. Gastreich saw seven or eight rounded and slightly oval, smooth, pea-sized shadows. Lyding reported twelve such shadows in the orbit in his case. Such shadows are well known to occur in the defective walls of cerebral vascular beds, such as arteriovenous aneurysms in the cranial and orbital cavities, and doubtless these calcifications are of similar origin. In our case there were two calcified plaques in the outer orbit (fig 2).

*Treatment and Pathologic Features*—Rychener (1942) observed improvement in a case reported by Chapman (1931) and later by Ellett (1940).

The injection of sclerosing solutions into the orbital veins has been advocated by several authors. Hippert noted successful results in 4 cases, Ravardino reported a success, but Dunphy, a failure.

The first operative attack on the large veins of the orbit for intermittent exophthalmos was made by Schimanowsky (1907). Through an incision under the eyebrow, he clamped and twisted the large vein, perhaps the superior ophthalmic, in the back of the orbit and allowed the clamp to remain two days before being withdrawn. Cure of the exophthalmos resulted, but with ptosis and ophthalmoplegia, the state of vision was not given. Three years later he operated in another case in similar fashion except that he tied and cut the veins. Precisely the same result was obtained. Lowenstein (1911), through a modified Kronlein approach, palpated venous tortuosities on the way to the supra-orbital vein. Bleeding was severe, it was controlled by the Paquelin cautery, and the wound was packed. During the next few days the exophthalmos was extreme but gradually disappeared by the twelfth day, four days later there was an enophthalmos of 3.5 mm, and this persisted. Slight exophthalmos (1.5 mm) persisted during jugular compression. The inferior rectus muscle was paralyzed, vision was greatly reduced immediately after operation but returned to 4/10 in four weeks and to 10/10 in nine weeks.

German and Weill explored the orbit of a patient who had had a retrobulbar hemorrhage and exhibited pronounced exophthalmos. A large number of dilated veins were observed within the muscle cone. In the attempt to isolate and ligate these veins there was spontaneous hemorrhage. Excision of the veins was performed. The exophthalmos was relieved. Two months later, the eye was enophthalmic, and there was external ophthalmoplegia. The state of vision was not recorded.

The only other case in which operation was done was reported by Rumjanzewa (1930), and a perfect result was obtained. The ophthalmic vein was ligated in the orbit through a supra-orbital incision, the exophthalmos was cured, without extraocular palsies. The author called it Golowin's operation—a method of attack used by him on pulsating exophthalmos.

In none of these records of operations is there any mention of pathologic observations except that the veins were large. The exposure of the orbit is doubtless too restricted to permit definition of any clearcut lesion, on the other hand, there is probably nothing in the orbit except large veins. The operation used in our case, as previously detailed, was a transcranial approach.

which has been evolved for orbital tumors. Since the lesion was intracranial and of a well recognized type, and since it was obliterated intracranially, there was no indication for removal of the orbital roof to inspect the orbit. This approach revealed the only extraorbital lesion that has been identified with intermittent exophthalmos. Had the orbit been explored by a Kronlein approach, the character of the underlying lesion would not have been disclosed. This arteriovenous aneurysm (not a single fistula, but coils of vessels replacing capillaries, with a larger lumen and of congenital origin) is of exactly the same character as are all arteriovenous aneurysms within the substance of the brain. Several cases of these aneurysms are cited in a paper published by one of us in 1928,

different types may be responsible for this unusual syndrome.

However, there is a serious risk in ligating large veins ahead of an arteriovenous aneurysm. In 1 of our cases of cerebral aneurysm (fig 4) another nearby vein ruptured. It must be realized that the great venous bed emerging from the arteriovenous coils is made as an adjustment to the entering arterial blood, and reduction in the bed throws a strain on the remaining veins, all of which have relatively weak walls.

#### COMMENT

In our case there could be no preoperative doubt that an arteriovenous aneurysm was causing this syndrome, i e., in view of the pulsation of the eyeball. Nor could it be doubted that it



Fig 4—Arteriovenous aneurysm of the brain, fundamentally similar to that presented in this paper (from Dandy, 1928, fig 4)

two photographs of such aneurysms are included here (figs 4 and 5)

We do not suggest that the treatment carried out in our case is the best solution of the problem. On the contrary, the result obtained by Rumjanzewa is so much better that in another case we should probably be content to ligate the superior ophthalmic vein and leave the aneurysmal coils alone. The surgical attack is much better, and there is consequently less risk of injuring the extraocular muscles through the transcranial than through either the Kronlein or the frontal approach. The ultimate decision concerning the best type of surgical treatment will, of course, be evolved only after greater experience and after it is known whether lesions of

was a "coiled" rather than a carotid-cavernous aneurysm (a fistula), which gives entirely different signs and symptoms, i e., a murmur, constant exophthalmos and dilated, pulsating vessels in the conjunctiva and over the forehead. There are never alternating exophthalmos and enophthalmos with a fistula, nor does jugular compression affect the protrusion of the eye. The coexisting enophthalmos was new in our experience but was assumed to be due to atrophy from pressure of the dilated veins. It is noteworthy that the space-occupying mass i e., the vascular coils, were almost entirely in the cranial chamber and not in the orbit. If this mass, as large as a walnut, had been in the orbit, there would have been constant exophthalmos and

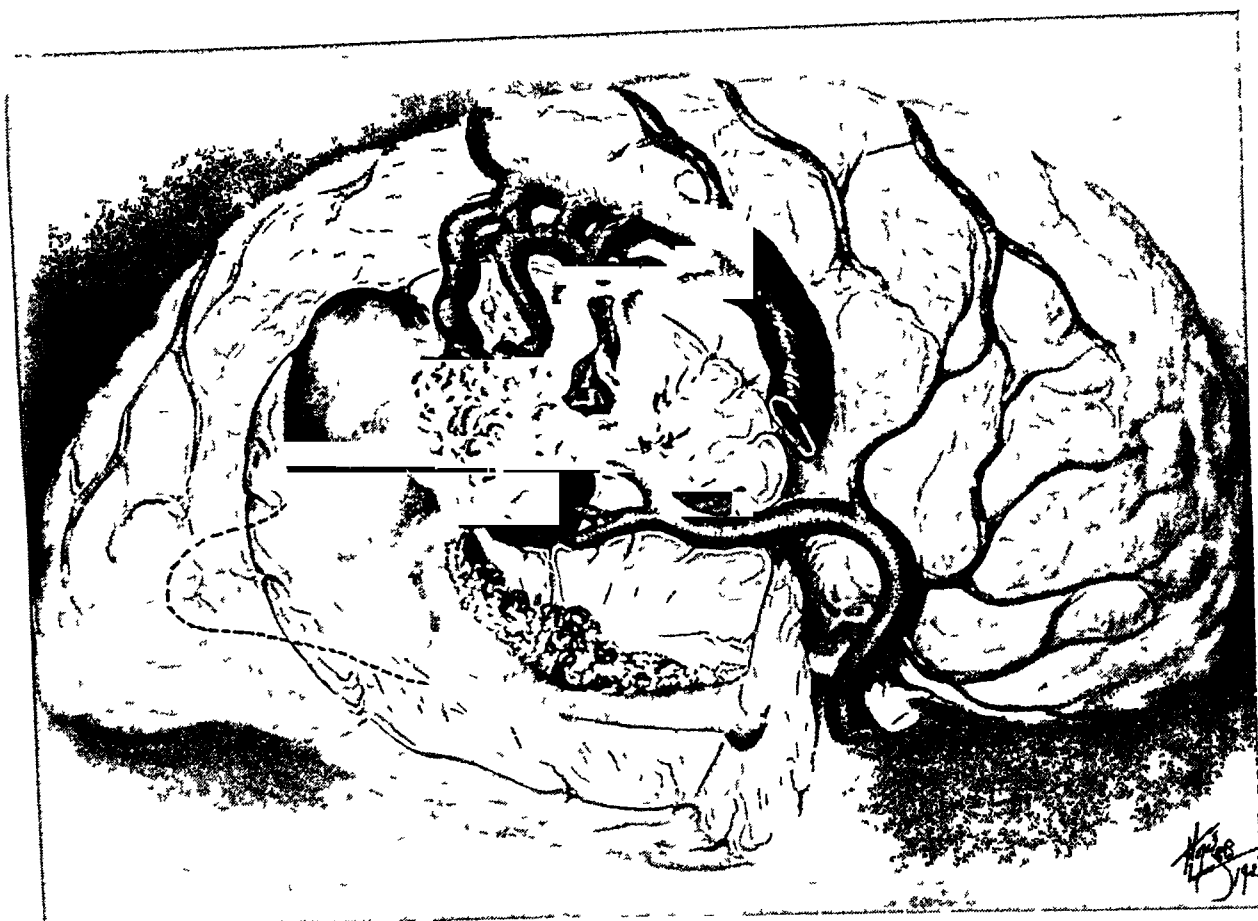


Fig 5—Reconstruction of an arteriovenous aneurysm, showing a coil of vessels which carry arterial blood and from which the tremendously enlarged veins emerge (from Dandy, 1928, fig 14) This drawing is shown because it is exactly like the arteriovenous aneurysm described in this paper





never enophthalmos. Only the enlarged veins that drained the aneurysm were in the orbit, and the size of these vessels changed with the volume induced by gravity and other physiologic factors affecting venous pressure largely through the corresponding jugular vein.

A glance at figures 4 and 5 will show the tremendous effect of arterial pressure on the size of the veins emerging from a cerebral arteriovenous aneurysm, the effect on the vein from an orbital or extraorbital aneurysm of similar type will be of precisely the same character.

It is not clear how far the pathologic changes in this case can be applied in all cases of intermittent exophthalmos. In all cases with pulsation of the eyeball there is doubtless just such a causative lesion. But in many, perhaps in the majority, of reported cases the pulsation either was not present (as determined by special mention of its absence) or was missed by the examiner. At least there must always be a large venous bed, but we know of no description of such large venous masses in the orbit. While purely venous aneurysms occur in the brain, they are uncommon, and they are not known to enlarge progressively. A true angioma would not be quickly influenced by changes in jugular pressure but would act simply as a space-occupying mass, producing a constant exophthalmos.

Until there are more pathologic confirmations of the underlying lesions in this condition, a conclusion applicable to all cases is clearly impossible.

It is possible that there are two general types of lesions causing intermittent exophthalmos, (1) arteriovenous with pulsation and (2) venous without pulsation, but speculation on this score is useless. The existence of the arteriovenous type at least is certain, that of the venous type is problematic. It is our guess that ocular pulsation has been overlooked in many cases. It is never so pronounced as in the usual pulsating exophthalmos from a carotid-cavernous fistula.

Arteriovenous aneurysm is, of course, a congenital maldevelopment, and never of traumatic origin. This accounts for its early appearance in most recorded cases. It might be asked why it is not present at birth. The answer is that the sustained arterial blood pressure causes the gradually progressive venous enlargement as the vascular coils with defective walls steadily dilate. The exact time of appearance of the syndrome, therefore, depends on the resistance of these walls, which must have wide individual variations. Doubtless many open in later life.

## CONCLUSIONS

In a typical case of intermittent exophthalmos the underlying lesion was observed at operation—a transcranial approach—to be an intracranial arteriovenous aneurysm lying in and behind the sphenoid fissure. This case is the only one in the literature in which a cause for this rare syndrome has been disclosed. The source of the arterial part of the aneurysm is not certain, it was thought to be the middle meningeal artery.

An arteriovenous aneurysm of similar type is probably responsible in all cases for pulsation of the eyeball. In most recorded cases pulsation was absent or missed. Whether or not there are two types of this syndrome, one with and the other without pulsation, cannot be determined without subsequent pathologic studies. Doubtless, in some cases the pulsation was present but was missed by the observer.

The intermittent exophthalmos was cured by obliterating the aneurysm with the electrocautery, but blindness of the affected eye and ophthalmoplegia resulted.

## BIBLIOGRAPHY

- Bartók, I. Exophthalmos intermittens (case 97), abstracted, *Zentralbl f d ges Ophth* **25** 225, 1931.
- Birch-Hirschfeld, A. Der intermittierende Exophthalmus, in Graefe, A., and Saemisch, E. T. *Handbuch der gesamten Augenheilkunde*, ed 2, Berlin, Julius Springer, vol 9, pt 1, 1917, chap 13, pp 105-149.
- Intermittierender Exophthalmus (Varix orbitae), in Schneck, F., and Bruckner, A. *Kurzes Handbuch der Ophthalmologie*, Berlin, Julius Springer, 1930, vol 3, pp 16-19.
- Byers, W. G. M. A Case of Intermittent Exophthalmos, *Arch Ophth* **50** 569-573, 1921.
- Chapman, T. C., cited by Rychener [case 98].
- Dandy, W. E. Arteriovenous Aneurysm of the Brain, *Arch Surg* **17** 190-243 (Aug) 1928.
- Orbital Tumors, New York, Oskar Priest, 1941.
- Delord, E., and Viallefont, H. Sur un cas d'exophthalmie intermittente, *Ann d'ocul* **169** 730-744, 1932.
- De-Petri, M. Sugli esoftalmi intermittente e pulsante e sulla loro terapia [case 99], *Riv oto-neurol-oftal* **12** 306-338, 1935.
- de Schweinitz, G. E. *Diseases of the Eye* Philadelphia, W. B. Saunders Company, 1924, pp 681-682.
- de Vincentis, C. Sull'esoftalmo da neoplasia dell'orbita, da ematoma orbitario, pulsante spontaneo e traumatico, di un moncone atrofico per aneurisma dell'arteria oftalmica, su di un occhio congenitamente pulsante, *Atti d r Accad med-chir di Napoli* **48** 367-464, 1894.
- Dunphy, E. B., in discussion on Poole, pp 116-117, case 109.
- Ellett, E. C. Unilateral Exophthalmos. *Tr A M A*, Sect Ophth pp 50-91, 1940, *J A M A* **116** 1-7 (Jan 4) 1941.
- Gastreich, C. Phlebolithen bei Orbitalvarizen mit intermittierendem Exophthalmus, *Klin Monatsbl f Augenh* **88** 773-777, 1932.
- Germain, L., and Weill, G. Les exophthalmies d'origine veineuse, *Bull Soc d'opht de Paris*, 1927, no 9, pp 594-597.

- Giqueaux, R. Varicocele de la orbita [case 107], *An argent de oftal* **3** 25-28, 1942
- Hippert, F. Deux cas d'exophtalmie intermittente. Le varicocele de l'orbite (Exophtalmie intermittente [cases 101 and 102], *Arch d'opht* **53** 135-146, 1936
- Kraupa, E, and Mendl, K. Ueber intermittierenden Exophtalmus, *Ztschr f Augenh* **89** 40-50, 1936
- Krauss, W. Beitrage zur Anatomie, Physiologie und Pathologie des orbitalen Venensystems zugleich uber orbital Plethysmographie, *Arch f Augenh* **66** 163-204 and 285-328, 1910
- Lindenmeyer, O. Ueber Exophtalmus intermittens, *Klin Monatsbl f Augenh* **68** 199-203, 1922
- Lipovich, N. Abwechselnder Ex- und Enophtalmus [case 104], *Sovet vestnik oftal* **9** 710-711, 1936 abstracted, *Zentralbl f d ges Ophth* **38** 279-280 1937
- Lowenstein, A. Ein Fall von operative geheiltem, sogenannten intermittierenden Exophtalmus, *Klin Monatsbl f Augenh* **49** 183-191, 1911
- Lyding, H. Demonstration eines Falles von Phlebolithen bei intermittierendem Exophtalmus, *Klin Monatsbl f Augenh* **90** 245-246, 1933
- Mann. Ueber den Mechanismus der Blutbewegung in der Vena jugularis interna, *Ztschr f Ohrenh* **40** 354-359, 1901-1902
- Ein neuer Beitrag zur Lehre vom Mechanismus der Blutbewegung in der Vena jugularis interna, *Verhandl d deutsch otol Gesellsch* **13** 121-128, 1904
- Marchesini, E. Su una rara forma di esoftalmo intermittente con atrofia discendente del nervo ottico (Contributo clinico alla diagnosi differenziale ed alla patogenesi) [case 100], *Ann di ottal e clin ocul* **63** 263-280, 1935
- Muirhead, W M. Intermittent Exophtalmos [case 103], *Tr Ophth Soc U Kingdom* **56** 304, 1936
- Mulder, M E. Ueber intermittierenden Exophtalmus mit Pulsation des Auges, *Klin Monatsbl f Augenh* **38** 3-13, 1900
- Petrov, A A. Ein Fall von einseitigem intermittierendem Exophtalmus [case 105] *Vestnik oftal* **14** 76-77, 1939, abstracted, *Zentralbl f d ges Ophth* **44** 674, 1939-1940
- Poole, W A. Intermittent Exophtalmos. Case Report [case 108], *Tr Am Acad Ophth* 112-118, 1942
- Radswitzki, P I. Ein Fall von Enophtalmus mit intermittierenden Exophtalmus, *Med obozr* **47** 726-732, 1897, abstracted, *Centralbl f Augenh*, 1897, p 642
- Ravardino. Guarigione di un caso di esoftalmo intermittente da varici dell'orbita, *Atti Cong Soc ital di oftal*, 1924, p 292, cited by Birch-Hirschfeld (1930)
- Reese, A B. Exophtalmos. Ocular Complications. Causes from Primary Lesions in the Orbit, *Surgical Treatment*, *Arch Ophth* **14** 41-52 (July) 1935
- Rones, B, in discussion on Poole, p 118 (case 110)
- Rumjanzewa, A F. Ueber den intermittierenden Exophtalmus und dessen operative Behandlung, *Ztschr f Augenh* **71** 247-253, 1930
- Rychener, R O, in discussion on Poole, pp 117-118
- Sattler, R. A Case of One-Sided Transitory Exophtalmos with Undisturbed Function and Muscular Movements of the Eye and the Coexistence of Enophtalmos or Recession of the Globe, *Am J M Sc* **89** 486-489, 1885
- Schimanowsky, A, cited by Rumjanzewa
- Spektor, S A. Intermittent Exophtalmos [case 106], *vestnik oftal* (no 5) **15** 73-75, 1939, abstracted, *Am J ophth* **23** 1070, 1940
- Weisner, E. Zwei Falle von intermittierendem Exophtalmus, *Klin Monatsbl f Augenh* **78** 163-165, 1927
- Wissmann, R and Schulz, A. Ueber intermittierenden Exophtalmus, *Arch f Augenh* **91** 11-33, 1922

# KERATECTOMIES FOR TREATMENT OF CORNEAL OPACITIES

RAMÓN CASTROVIEJO, M D

/ NEW YORK

The surgical treatment of corneal opacities has been in use for over two centuries Boury,<sup>1</sup> in 1743, Plenck,<sup>2</sup> in 1783, Bertlandi,<sup>3</sup> in 1798, Wenzel,<sup>4</sup> in 1808, Demours,<sup>5</sup> in 1821, Rosas,<sup>6</sup> in 1830, Carron du Villards,<sup>7</sup> in 1838, Chelius,<sup>8</sup> in 1839, Cappelletti,<sup>9</sup> in 1844, and Desmarres,<sup>10</sup> in 1847, spoke of scarifications and abrasions of the cornea. Small, nonperforating punctures made with a knife or needles in the cornea in order to provoke inflammatory processes tending to clear up the opacities were advocated by Ware,<sup>11</sup> in 1795, by Holchers,<sup>12</sup> in 1842, and by Himley,<sup>13</sup> in 1843. Riveri,<sup>14</sup> in 1836, advocated paracentesis of the anterior chamber to improve the vision of eyes with corneal opacities, especially those with abundant vascularization.

Another surgical procedure used to improve vision in eyes affected with corneal opacities consists in the excision of the superficial lamella of the opaque cornea. This method was advo-

cated by Chevalier Taylor<sup>15</sup> in the early part of the eighteenth century, by Boury,<sup>1</sup> in 1743, by Platner,<sup>16</sup> in 1747, by Pellier,<sup>17</sup> in 1783, by Gouan,<sup>18</sup> in 1783, by Bell,<sup>19</sup> in 1788, by Malgaigne,<sup>20</sup> in 1843, by Cappelletti,<sup>9</sup> in 1846, by Guepin,<sup>21</sup> in 1847, and by Denovillers<sup>22</sup> and Gosselin,<sup>23</sup> in 1855. Others who, without advocating this method, described it are Duddell,<sup>24</sup> in 1729, Mead,<sup>25</sup> in 1775, Scarpa,<sup>26</sup> in 1809, and Mackenzie,<sup>27</sup> in 1854. In 1846 Donders<sup>28</sup> studied the regeneration of corneal tissue after excision, reporting that when one half or two thirds of the superficial layers of the cornea are removed, healing occurs without inflammation or any other abnormality.

Some of the methods of corneal excision described by the aforementioned authors resemble remarkably surgical procedures which have been described in the past thirty or forty years. Those who have been interested in the excision of cor-

From the Institute of Ophthalmology, Columbia-Presbyterian Medical Center

1 Boury, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, pp 294-295

2 Plenck, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 294

3 Bertrandi, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 294

4 Wenzel, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 294

5 Demours, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 294

6 Rosas, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

7 Carron du Villards, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

8 Chelius, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

9 Cappelletti, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

10 Desmarres, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

11 Ware, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

12 Holchers, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

13 Himley, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

14 Riveri, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

15 Taylor, J. (Chevalier), cited by James, R. R. *Studies in the History of Ophthalmology in England Prior to the Year 1800*, London, Cambridge University Press, 1933, p 188

16 Platner, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

17 Pellier, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

18 Gouan, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

19 Bell, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

20 Malgaigne, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

21 Guepin, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

22 Denovillers, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

23 Gosselin, cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, vol 1, p 295

24 Duddell, B., cited by James, R. R. *Studies in the History of Ophthalmology in England Prior to the Year 1800*, London, Cambridge University Press, 1933, pp 93, 97 and 151

25 Mead, cited by James<sup>37</sup>

26 Scarpa, A., cited by Ovio, G. *L'oculistica di Antonio Scarpa*, Naples, V. Idelson, 1936, *Traite pratique des maladies des yeux*, Paris, Meguignon-Marvis, 1821, pp 350-351

27 Mackenzie, W., cited by James<sup>37</sup>

28 Donders, F. C. *Untersuchungen über die Regeneration der Hornhaut*, Holland Beitr zu d anat. u physiol Wissensch 1 387-400, 1846-1848

neal scars in more recent years are Jobson,<sup>29</sup> in 1909 and 1912, Wiener<sup>30</sup> in 1909, 1926 and 1939, Zentmayer,<sup>31</sup> in 1909, Rucker,<sup>32</sup> in 1929, Goar,<sup>33</sup> in 1931, Hilgartner Sr and Jr,<sup>34</sup> in 1931 and 1937, Castroviejo,<sup>35</sup> in 1937, Verhoeff,<sup>36</sup> in 1939, and James,<sup>37</sup> in 1942

Still another surgical procedure advocated for the treatment of corneal opacities is corneal transplantation. Since the number of surgeons who have written about the surgical treatment of corneal opacities is large, it will not be possible to describe in this paper their operative technics. Readers who are interested in more detailed information about the previous work on this subject are referred to the original publications of the authors mentioned.

Among the corneal opacities covering the pupillary area there are some susceptible of treatment by corneal transplantation, which gives the best results as far as improvement of vision is concerned. Other opacities are unfavorable for keratoplasty on account of excessive density of the scar or pronounced superficial vascularization, which would render the transplant nebulous or opaque. Corneas affected by dystrophia adiposa and other forms of dystrophy are unfavorable for keratoplasty because the disease process invades the transplant, rendering it nebulous or opaque.

There are other superficial opacities in the pupillary area which, although lending themselves to satisfactory treatment by corneal transplanta-

tion, are best handled by other surgical procedures which expose the eye to fewer complications. Recurrent pterygium, pseudopterygium and symblepharon, especially when they have invaded the pupillary area, do not lend themselves well to corneal transplantation.

For some of these conditions for which corneal transplantation is not indicated, superficial keratectomy is the preferred procedure. Keratectomy may be partial, when only a limited area of the external lamella of the cornea is excised or total, when the excision extends over the whole area of the cornea.

It is not the purpose of this article to give statistics for patients subjected to keratectomies; this will be the object of a future publication. At present I shall limit myself to a brief description of the different types of keratectomy which I have been using for the past few years, justifying this preliminary report by the usefulness which this type of surgical treatment may have in repairing the ocular sequela of war injuries.

The illustrations used in this article have been taken from moving pictures of the operations. The photographs illustrating the different steps of the operations have been retouched in order to eliminate confusing reflexes and shadows. The photographs illustrating the postoperative results are not retouched.

#### 1 PARTIAL SUPERFICIAL KERATECTOMY FOR THE TREATMENT OF BAND KERATITIS

This operation may be carried out with either general or local anesthesia. After the speculum is inserted, the eye is fixed with O'Brien or Elschning forceps. The area of the cornea to be excised, including the opacity extending across the pupillary area, is outlined by two incisions made with the Graefe knife above and below the opacity, the incisions penetrating approximately one-third the depth of the cornea (1). The incisions outlined with the knife can be made more visible by the instillation of a 2 per cent solution of fluorescein sodium. Dissection of the superficial layers of the cornea, including the opacity, is started on the temporal side with the aid of the Graefe knife (2), the edge of the corneal flap being held with fine conjunctival forceps or, better yet, with jeweler's forceps, which are strong and have very fine points. The dissection of approximately the outer third of the corneal thickness, including the opacity, is carried out with the aid of a Graefe knife from the temporal to the nasal side, until the limbus is reached (3). At the limbus, the corneal flap thus dissected is excised with scissors (4), so that the pupillary area is left transparent (5). The operation is concluded with

29 Jobson, G. B. Report of a Case of Nodular Opacity of the Cornea Cured by Excision, *Tr Am Acad Ophth* **14** 300-302, 1909, Keratectomy for Removal of Corneal Scars and Opacities, *Ophth Rec* **21** 332-336, 1912.

30 Wiener, M. (a) Regeneration of the Cornea, *J A M A* **53** 762-764 (Sept 4) 1909, (b) in *Contributions to Ophthalmic Science*, Menasha, Wis., George Banta Publishing Company, 1926, p 193. Wiener, M., and Alvis, B. Y. *Surgery of the Eye*, Philadelphia, W. B. Saunders Company, 1939, pp 157-166.

31 Zentmayer, W., in discussion on Wiener<sup>30a</sup>

32 Rucker, C. W. Regeneration of the Cornea, *Arch Ophth* **2** 692-698 (Dec) 1929.

33 Goar, E. L. Nodular Dystrophy of the Cornea, *Am J Ophth* **14** 133, 1931.

34 Hilgartner, H. L., Jr., and Hilgartner, H. L. Preliminary Report of Twenty-Three Cases of Corneal Opacities Treated with Surgery and Radium, *South M J* **24** 574-579 (July) 1931, Nodular Dystrophy of the Cornea Six Years After Treatment with Corneal Resection and Radium. Report of a Case, *Am J Ophth* **20** 387-389 (April) 1937.

35 Castroviejo, R. Surgery of the Cornea, *Internat Abstr Surg* **65** 489-505, 1937, in *Surg, Gynec & Obst* December 1937.

36 Verhoeff, F. H., in discussion on Lloyd, R. I. Lattice Dystrophy of the Cornea, *Tr Am Ophth Soc* **37** 120-126, 1939.

37 James, W. M. The Surgical Removal of Corneal Scars, *Am J Ophth* **25** 672-684 (June) 1942.

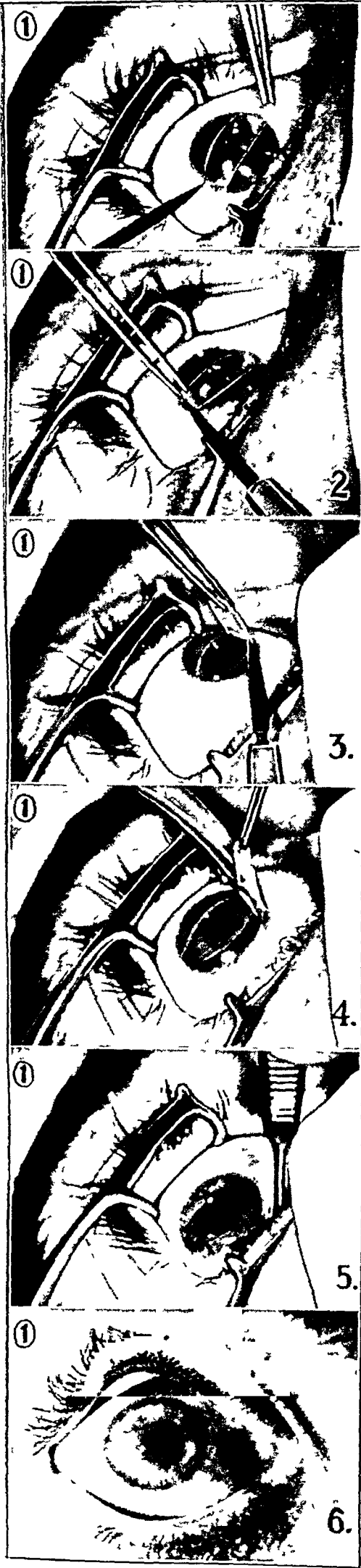


Fig 1—Steps 1 to 6



Fig 2—Steps 7 to 12

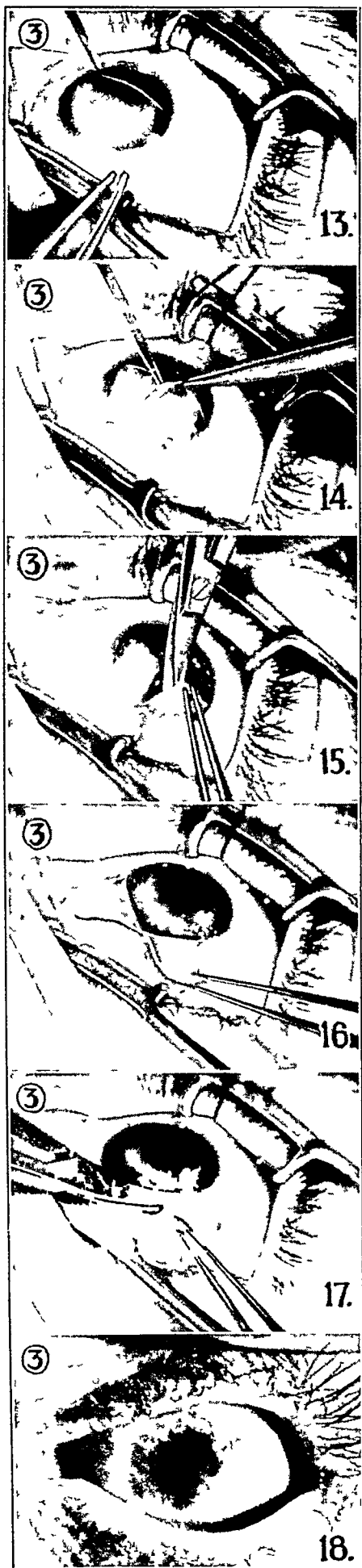


Fig 3—Steps 13 to 18

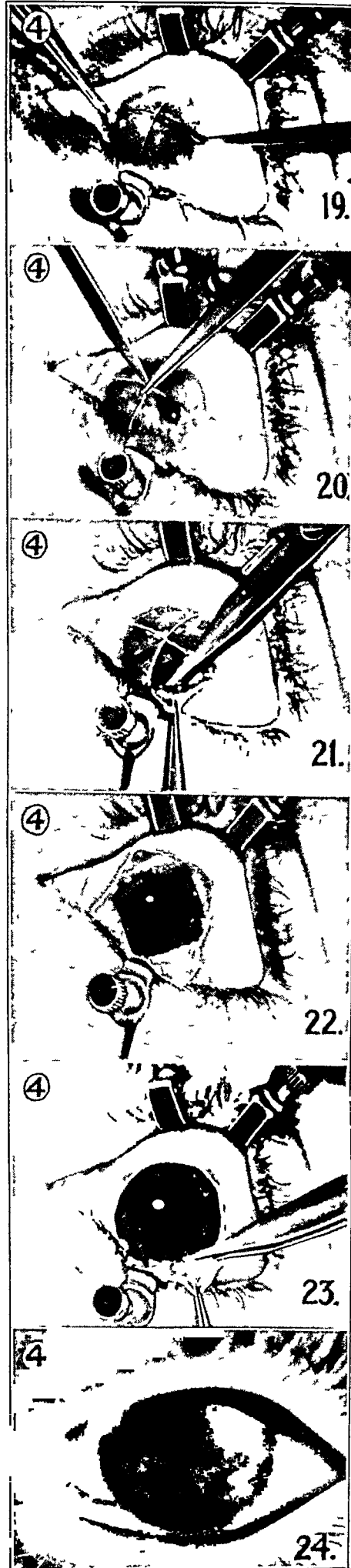


Fig 4—Steps 19 to 24

the application of an antiseptic ointment, such as metaphen (1 3,000) or, better yet, penicillin ointment,<sup>38</sup> containing 500 Oxford units per gram, and a monocular dressing. The eye is dressed daily, with instillation of a 2 per cent solution of fluorescein sodium to observe the progress of the epithelization of the cornea, and the application of an ointment of metaphen or penicillin. If there is ciliary injection, it is advisable to instil atropine sulfate, in 1 per cent solution.

As a rule, the cornea is completely epithelized in from four to seven days, and the eye may be uncovered. In about two weeks the eye is quiet, the pupillary area remains transparent (6), and improvement of vision is considerable (from ability to see hand movements or count fingers at a few centimeters to an acuity of 20/200 or better). For several months after the operation there is likely to be considerable irregular astigmatism, which later tends to diminish.

## 2 PARTIAL SUPERFICIAL KERATECTOMY FOR TREATMENT OF DYSTROPHIA ADIPOSA CORNEAE

This operation may be performed with general or local anesthesia. After insertion of the speculum or of a substitute, such as the mosquito lid clamp retractors shown in the illustrations, the eye is fixed with forceps. The upper limit of the corneal area to be excised is outlined with the aid of the Graefe knife (7), the incision penetrating approximately one-third the depth of the cornea. The incision made with the knife is better visualized by the instillation of a 2 per cent solution of fluorescein sodium. The dissection of the superficial layers of the cornea, including the opacity, is started with the aid of the Graefe knife while the lip of the corneal flap is held with fine conjunctival forceps or with jeweler's forceps (8). With the aid of scissors with blunt points,<sup>39</sup> the dissection is extended to the limbus (9). The flap of cornea thus obtained, including approximately the outer third of the corneal thickness and the opacity, is excised at the limbus with the aid of scissors (10). The pupillary area thus uncovered contains only healthy, transparent corneal tissue (11). The operation concludes with the application of an antiseptic or a penicillin ointment and a monocular dressing.

The postoperative treatment is carried out as described in the previous operation. The results obtained with this method are similar to those obtained with the operation previously described for the treatment of band keratitis. Several

weeks after the operation the pupillary area may be expected to be clear (12), with considerable improvement of vision. In these cases of dystrophia adiposa corneae it is advisable to carry out a thorough investigation of the patient's general condition to find out whether there is any systemic cause which might influence the recurrence of the ocular lesion. If any such cause is found, it should be corrected. The operation just described is also indicated for other types of corneal dystrophy involving only the external layers of the cornea.

## 3 PARTIAL SUPERFICIAL KERATECTOMY FOR TREATMENT IN LEUKOMA

Eyes favorable for this type of operation are those in which, as a sequel of infection or trauma, scars have developed over a limited area of the superficial cornea. The operation is similar to the two previously described and can also be undertaken with local or general anesthesia. After insertion of the speculum and fixation of the eye with forceps, a Graefe knife is used to limit the corneal area to be dissected (13). With the same knife, another incision is made perpendicular to the first one, in order to divide the area to be excised into two flaps (14). If the edge of the corneal flaps is held with the jeweler's forceps, from one third to one half of the external layers of the cornea (depending on the depth of involvement of the cornea by the leukoma) is dissected away, the incision being begun with a Graefe knife (14) and continued with scissors (15) until the limbus is reached. When the two flaps thus outlined have been dissected down to the limbus (16), they are excised at the limbus with scissors (17). The operation ends with the application of an antiseptic or a penicillin ointment. The postoperative course resembles that outlined for the operations previously described.

The improvement of vision obtained by this operation depends on the extent of the leukoma into the corneal-stroma. A few weeks after the operation the eye is usually quiet, and the appearance (18) and vision are considerably improved. If, after excision of the leukoma by the technic of the partial keratectomy just described, vision should not improve as much as desired, the eye, which before the keratectomy was unfavorable for keratoplasty, is rendered more favorable for this type of surgical procedure.

## 4 TOTAL SUPERFICIAL KERATECTOMY FOR TREATMENT OF VASCULARIZED LEUKOMA

This operation may be performed on eyes in which superficial vascularized scars have developed after severe injuries or infections. The operation may be performed under local or general

<sup>38</sup> The penicillin ointment, with a jelly base, was supplied by E. R. Squibb & Sons.

<sup>39</sup> The special scissors used for this operation, and for subsequent operations, are manufactured by V. Mueller & Co., Ogden Ave., Chicago.



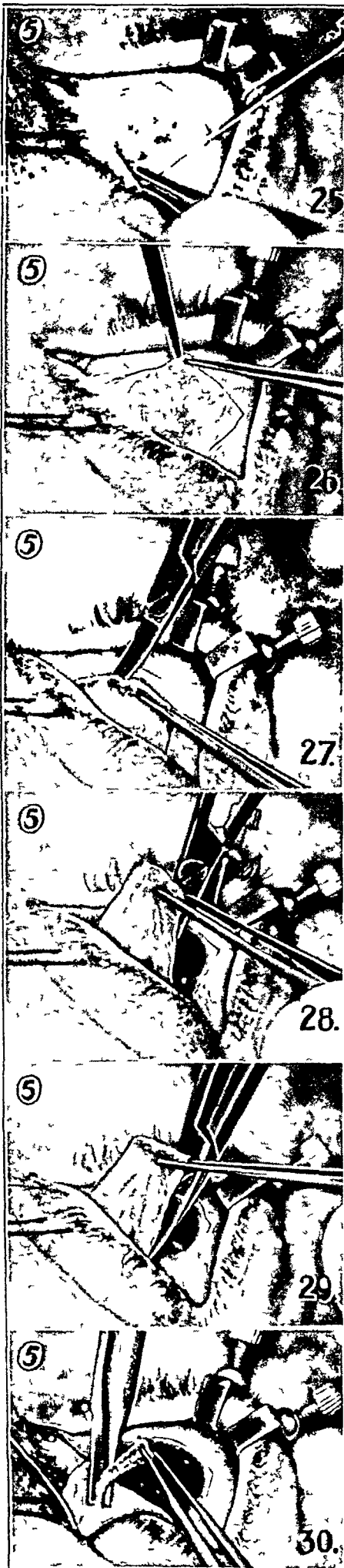


Fig 5—Steps 25 to 30

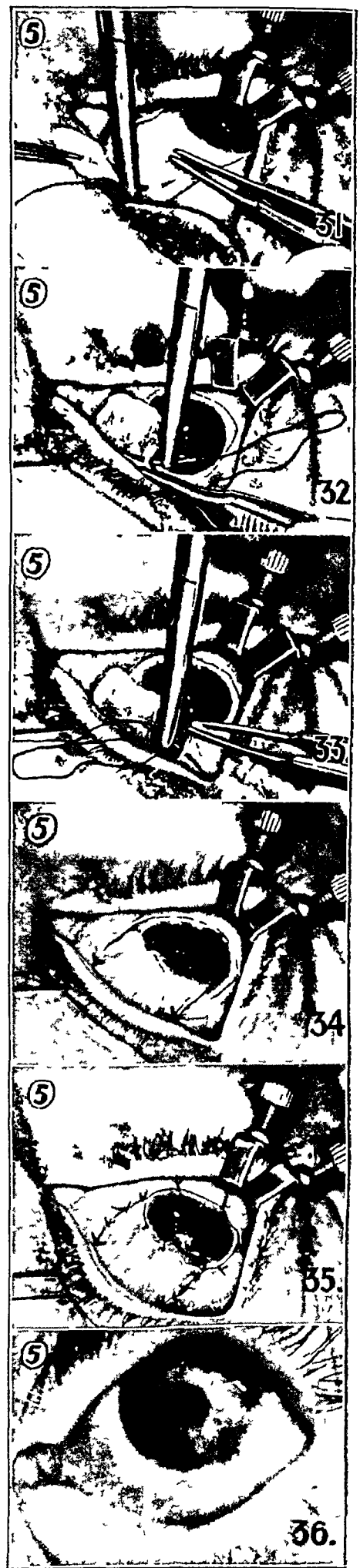


Fig 5 (Continued) —Steps 31 to 36

anesthesia The procedure consists in making, with the aid of a Graefe knife, a crucial incision in the cornea extending from limbus to limbus and to a depth of approximately one-half the corneal thickness (19) The four corneal flaps

corneal flaps have been dissected as far as the limbus (22), they are excised with scissors (23), the operation being finished with the application of an antiseptic ointment, such as metaphen or, better, penicillin ointment, and the application of a monocular dressing This

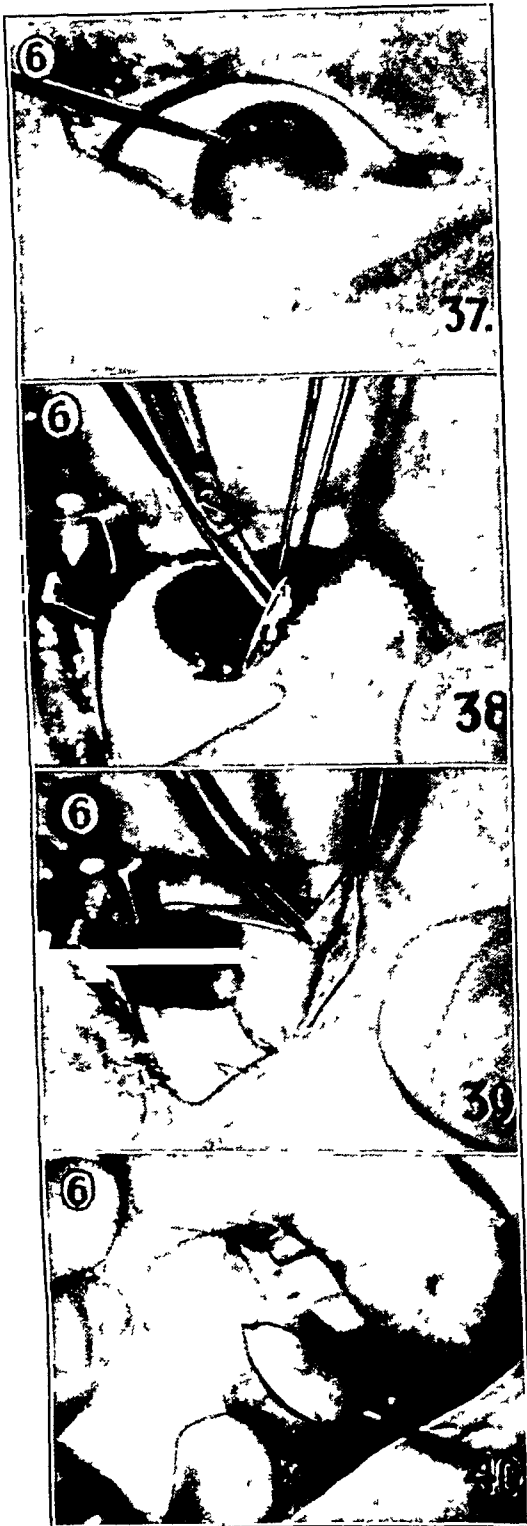


Fig 6—Steps 37 to 40

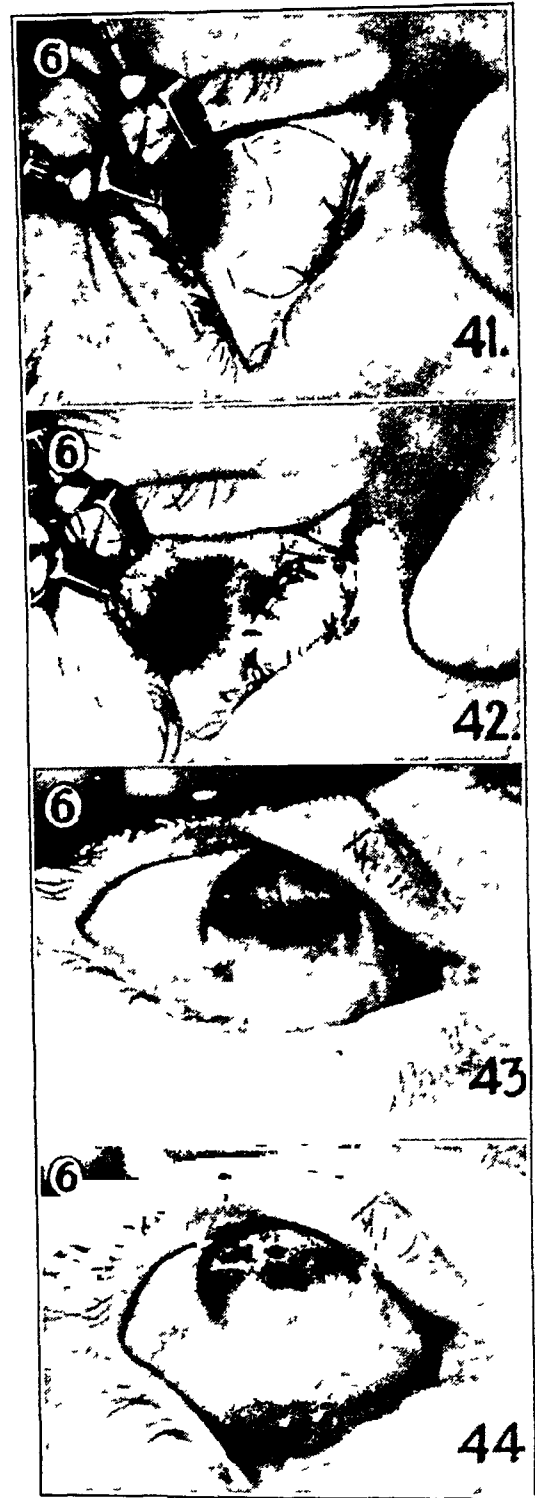


Fig 6 (Continued) —Steps 41 to 44

thus limited by the crucial incision are dissected as described in previous operations The dissection of approximately the outer half of the corneal thickness is begun with a Graefe knife, while the apex of the flap is held by the jeweler's forceps already mentioned in previous operations (20), and is continued with scissors, the same plane of cleavage being always maintained (21) until the limbus is reached When the four

operation was described by Wiener in 1926 The operation as described here differs from Wiener's only in that the apex of the corneal flaps is held with a jeweler's forceps instead of the hook he advocated Such a hook has, I believe, more tendency to tear the corneal tissue, especially when it is friable Another modification in this technic is the use of scissors with blunt points to complete the dissection of the corneal flaps,

instead of employment of the knife exclusively. Those who are experienced in this type of operation will be able to dissect the corneal flaps without difficulty with the exclusive use of the knife. For surgeons with less experience, the use of scissors with blunt points will facilitate the dissection

pital, under the direction of Dr Maurice Lenz. The eye is anesthetized by the instillation of a 0.5 per cent solution of tetracaine hydrochloride. A lid speculum is inserted, and the treatment is given directly to the open eye. A voltage of 100 kilovolts, with no filter, and a target skin

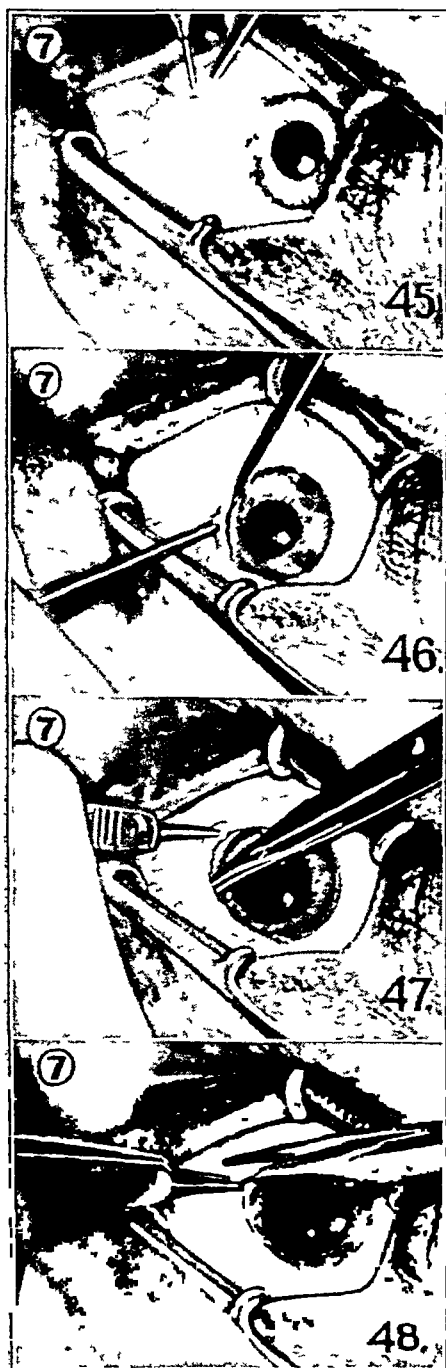


Fig 7—Steps 45 to 48

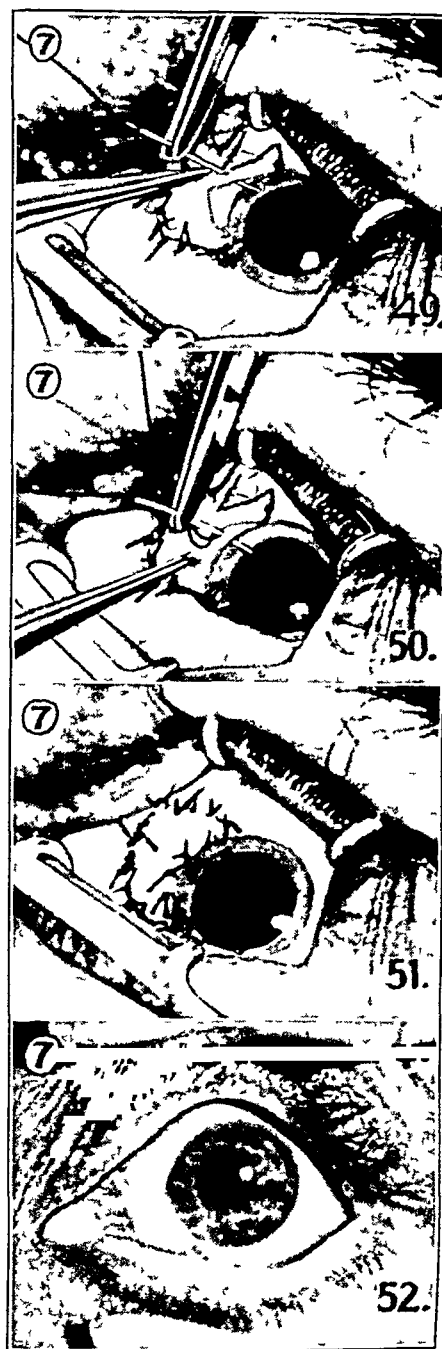


Fig 7 (Continued)—Steps 49 to 52

of the corneal flaps, with less danger of puncture of the inner layers of the cornea.

To prevent recurrence of corneal vascularization in these patients I have found it useful to give treatment with roentgen rays, the irradiation starting not later than twenty-four hours after the operation.

These patients have been treated in the department of radiotherapy of the Presbyterian Hos-

pital, under the direction of Dr Maurice Lenz. The eye is anesthetized by the instillation of a 0.5 per cent solution of tetracaine hydrochloride. A lid speculum is inserted, and the treatment is given directly to the open eye. A voltage of 100 kilovolts, with no filter, and a target skin distance of either 6 or 9 inches (15 or 23 cm) are used. The first treatment varies between 50 and 100 r, the dose depending on the postoperative inflammatory reaction. The following day, or two days thereafter, the interval again depending on the status of the eye, another 100 r is given. This is repeated every day or two until a total of 400 r has been given within the first week or ten days after the opera-

tion In cases in which, in spite of anesthesia, the treatment through the open eye is too painful, we have given the first and second treatments with the lids closed, using 130 kilovolts, a 2 mm aluminum filter and 100 r at each treatment To some patients thus treated, as much as 600 r in two weeks has been administered

Generally, ten days after the operation the cornea is fully epithelized, and at the end of one month the eye, as a rule, with little or no inflammation, appears as shown in 24, considerably improved both in appearance and in vision The latter may be expected to increase from light perception and projection or perception of hand movements at a distance of a few centimeters to an acuity of 10/200, 20/200 or better We have never observed a cataract caused by these roentgen treatments

Instead of the application of roentgen radiation to prevent recurrence of corneal vascularization, radium may be used I have had no experience with the application of radium for this purpose, but I have seen patients treated in the department of ophthalmology of the Johns Hopkins Hospital, under the supervision of Dr A C Woods The result of radium therapy in these cases seems to be similar to that in the cases in which we used roentgen rays I quote from the letter of Dr Charles E Iliff, describing the technic of radium application used at the Johns Hopkins Hospital

"My colleagues and I use beta radiation, employing the applicator designed by Dr Curtis Burnam, in 1925 This consists of a soda glass bulb, 0.5 mm in diameter, containing 250 to 500 millicuries of radon encased in two small brass cylinders, which have a 4 mm opening at one end The outer cylinder is fastened to a 35 cm handle for convenient application Through the 4 mm window all the beta radiation and most of the gamma radiation pass The proportion of beta to gamma radiation is 100 to 1, so we usually consider the applicator with regard to beta radiation alone

"The very soft beta rays are screened out by a heavy paper filter, or, if the lesion is superficial, unfiltered beta rays are used The dose ranges from 1 gram for six seconds to 1 gram for twelve seconds, usually for three weekly treatments, followed by a rest period of four to six weeks The course of therapy is then repeated until the desired effect is obtained

"We have never had a cataract produced by radiation, nor have we been able to find a

reference in the literature to one when beta radiation was used"

##### 5 TOTAL SUPERFICIAL KERATECTOMY AND CORNEOCONJUNCTIVAL PLASTIC FOR THE TREATMENT OF VASCULARIZED LEUKOMA AND SYMBLEPHARON

This procedure is better carried out with the patient under general anesthesia because the infiltration required for local anesthesia deforms the tissues and does not permit the performance of the different operative steps as cleanly as when the tissues, without the infiltration produced by the anesthetic, have remained undisturbed This operation is applicable to eyes with lesions similar to those described in the previous operation, but with the addition of symblepharon In this operation the palpebral fissure must be kept open by the application of mosquito lid clamp retractors and sutures, for the symblepharon does not permit the insertion of the speculum With the aid of a Graefe knife, a quadrangular flap is outlined by making a horizontal incision at the level of the upper limbus, followed by two vertical incisions, one starting at each end of the first incision and descending on the nasal and the temporal side tangential to the limbus to reach the borders of the symblepharon (25) The edge of the flap thus outlined is held with the aid of fine conjunctival forceps or jeweler's forceps, and the superficial layers of the cornea, including the vascularized scar tissue, are dissected, the dissection beginning with a Graefe knife (26) and then proceeding along the same plane of cleavage, with the aid of scissors with blunt points (27) Once the lower limit of the limbus has been reached with this dissection (28), the lateral incisions of the dissected corneal flap are continued temporally and nasally on each side of the symblepharon (29) until the lower fornix is reached The dissection just described had the double purpose of uncovering the transparent corneal tissue (thus rendering the eye useful for visual purposes) and of making a corneoconjunctival flap, which is to be used to complete the operation as follows The corneoconjunctival flap is thinned with the aid of scissors on its bleeding under surface, with the purpose of eliminating most of the connective tissue (30), which, if left would have a tendency to cause contraction and thickening of the flap The defect left in both the eyeball and the inner aspect of the lid is covered by means of the corneoconjunctival flap A double-armed 0000 silk suture mounted in an atraumatic needle is used to fix to the sclera,

at the point where the fornix is to be made (31), both the edge of the flap (32) and the edge of the conjunctiva (33) temporally and nasally (34). The rest of the border of the corneoconjunctival flap is sutured to the adjacent conjunctiva and to the limbus (35) by means of 000000 silk mounted in an atraumatic needle, care being taken to anchor all the stitches to the sclera, as well as to the limbus, to prevent cicatricial retractions and the possible recurrence of the symblepharon, which almost invariably would take place if the stitches were placed between the corneoconjunctival flap and the conjunctiva without scleral anchorage. The rest of the conjunctiva is anchored to the sclera around the limbus to prevent the conjunctiva from slipping over the cornea and cicatrizing in a faulty position over the cornea. The operation is finished with the application of an antiseptic ointment or, better, penicillin ointment. A monocular dressing is applied with moderate pressure to prevent the accumulation of blood and exudates under the flap. The postoperative treatment also includes the application of roentgen rays, as described in previous operations, to prevent the recurrence of corneal vascularization, and the daily application of an antiseptic or penicillin ointment until complete epithelization of the cornea has taken place. About ten days after the operation, the stitches which are still present in the eye are removed, with the use of local anesthesia. If no complications arise, about one month after the operation the eye shows slight reaction, if any (36), with complete correction of the symblepharon, so that the appearance of the eye, as well as the visual acuity, is considerably improved. Improvement of vision may be expected to be approximately the same as that obtained by the two previous surgical procedures. The same operation described for the correction of vascularized leukoma and symblepharon of the lower lid can be used for the upper lid.

6 PARTIAL SUPERFICIAL KERATECTOMY CORNEO CONJUNCTIVOPLASTY AND GRAFT OF BUCCAL MUCOUS MEMBRANE FOR THE TREATMENT OF VASCULARIZED LEUKOMA AND SYMBLEPHARON

Occasionally, in cases of severe symblepharon, covering a large part of the whole cornea, the tissue dissected from the cornea does not suffice to cover both the defect left in the eyeball and the inner surface of the lid. In this instance the following technic may be used.

The operation should be performed with the patient under general anesthesia, for the reasons given for the operation previously described.

With the aid of a Graefe knife (37), an incision is made in clear corneal tissue above the symblepharon to outline the upper limit of the corneal flap which is to be dissected. While the lip of the incision is held with fine conjunctival forceps or jeweler's forceps, approximately the external half of the cornea containing the symblepharon is dissected. The dissection started with the knife is completed down to the limbus with scissors (38). With the aid of scissors, incisions are made along the borders of the symblepharon, down to the lower fornix (39). The corneoconjunctival flap thus obtained is thinned by removing from its bleeding under surface as much as possible of the connective tissue. The corneoconjunctival flap thus obtained does not suffice to cover both the defect left on the eyeball and the defect in the inner aspect of the lid. The inner aspect of the lid is covered by the corneoconjunctival flap. The defect on the eyeball is covered with a graft of buccal mucous membrane obtained with the aid of a Graefe knife from the inner aspect of the lower lip (40). The incision made in the mouth is closed with interrupted sutures of 0000 silk. The graft of buccal mucous membrane must be thinned as much as possible in order to eliminate the connective tissue which tends to contract. The thinner the graft of buccal mucosa the more elastic it is, adapting itself better to the defect to be covered. Also, the thinner the graft the better is the cosmetic appearance. A thick graft has more tendency not only to contract but to remain thick and unusually red. The flap of buccal mucosa is placed on the eyeball to cover the defect. The edges of the buccal mucous membrane graft, as well as the corneoconjunctival flap, are fixed to the sclera (41) by means of three sutures placed where the lower fornix is to be located. The remaining margins of the flap of buccal mucosa are sutured to the adjacent conjunctiva and to the limbus by means of 000000 silk, the stitches being anchored to the sclera (42) to prevent cicatricial retraction and the possible recurrence of the symblepharon.

The operation ends with the application of an antiseptic or penicillin ointment. A monocular dressing is applied with moderate pressure to prevent the accumulation of blood and exudates under the graft and flap. The postoperative course is similar to that described for the previous operations, with the application of roentgen rays to prevent the recurrence of corneal vascularization. At the end of several weeks, the eye which was used to illustrate this operation showed a fairly transparent cornea in the pupillary area.

(43), with considerable improvement in appearance and slight improvement in visual acuity. The symblepharon was totally corrected (44). Cilia were restored to the border of the lower lid afterward by transplantation of a strip of brow to the lid. The corneal scar in the pupillary area was later successfully treated by corneal transplantation.

#### 7 PARTIAL SUPERFICIAL KERATECTOMY AND GRAFT OF BUCCAL MUCOUS MEMBRANE FOR THE TREATMENT OF RECURRENT PTERYGIUM

This operation may be performed with local anesthesia. Once the eye is anesthetized, a subconjunctival injection of a 2 per cent solution of cocaine with a 1:1,000 dilution of epinephrine hydrochloride is made beneath the pterygium (45). The superficial layers of the cornea, including the apex of the pterygium, are dissected from the cornea with the aid of a Graefe knife and jeweler's forceps (46). When the limbus is reached, the conjunctiva, which is generally solidly attached to the eyeball, is undermined with the aid of scissors (47). The edge of the pterygium containing the corneal tissue is excised (48), together with the excess of connective tissue which remains adherent to the pterygium after it has been separated from the eyeball. The defect left in the eyeball is covered with a graft of buccal mucous membrane obtained in the same fashion as that described for the preceding operation. The graft of buccal mucosa is sutured to the adjacent conjunctiva (49) and at the limbus (50, 51), the stitches being anchored to the sclera to prevent cicatricial retraction, as well as to avert the healing of the implant in a faulty position over the cornea. The operation ends with the application of an antiseptic or a penicillin ointment. A dressing is applied with moderate pressure to prevent the accumulation of blood or exudates under the implant. The postoperative course is like that in the cases previously described, the application of roentgen radiation being necessary to prevent the recurrence of corneal vascularization or the recurrence of the pterygium. Illustration 52 shows the eye two years after the operation, with no tendency to recurrence. The technic just described was advocated by H. Gifford,<sup>40</sup> in 1909, and by Duverger and Velter,<sup>41</sup> in 1926. These authors

did not suture the grafts of buccal mucous membrane to the sclera, and by this omission failed to prevent contraction of the graft.

#### SUMMARY

Superficial keratectomy in selected cases offers the ideal method of attempting to improve the visual acuity of the affected eyes. Penicillin ointment has been found to shorten the period of healing and reduce the occurrence of infection.

Dr. Maurice Lenz cooperated in the treatment of some of the patients, and Mr. Gustav Bethke helped in the preparation of the illustrations.

635 West One Hundred Sixty-Fifth Street

#### DISCUSSION

DR. F. H. VERHOEFF, Boston: Dr. Castroviejo's use of the symblepharon tissue to cover the defect in the lid is ingenious, and it is evident that his early postoperative use of roentgen irradiation was essential to his success in the cases he reports.

DR. WENDELL L. HUGHES, Hempstead, N. Y.: What was the final vision in the first case of keratitis, and was any radiation used? Did the ophthalmometric reading show any irregularity in the surface?

DR. E. V. L. BROWN, Chicago: What pathologic change was noted in the tissue removed in case of band keratitis?

DR. RAMÓN CASTROVIEJO: Keratectomy, meaning the excision of external layers of the cornea, is not a new procedure in cases of corneal opacities. More than one hundred and fifty years ago Scarpa described this operation in discussing corneal opacities, which he classified as nebula, albugo and leukoma. Superficial keratectomy as described in records of the past thirty or forty years remarkably resembles the surgical procedures described more than one hundred and fifty years ago. Wiener's technic of total superficial keratectomy would seem to produce irregularity of the pupillary area, and, therefore, visual acuity would not improve as much as might be expected. However, if the dissection is carried out carefully, evenness in the pupillary area can be obtained, with considerable subsequent improvement of vision.

In the case of band keratitis reported, visual acuity after the operation was 20/200. The patient had had severe iridocyclitis in both eyes. Pigment was scattered throughout the anterior surface of the lens, in sufficient amount to cause great impairment of vision. Shortly after the operation astigmatism was pronounced, but two years later the astigmatism had improved con-

<sup>40</sup> Gifford, H. The Treatment of Recurrent Pterygium, *Ophth. Rec.* 18:1-8, 1909.

<sup>41</sup> Duverger and Velter. *Therapeutique chirurgicale ophtalmologique*, Paris, Masson & Cie, 1926, pp. 124-128.

siderably The excised cornea in this case was sent to the laboratory for study, but since at that time I was concerned chiefly with improvement of the patient's vision, I did not study the pathologic report, which probably indicated the usual changes in cases of this type

If corneal opacities still remain after the first dissection, a second dissection can be carried out to remove another portion of the external

layers of the cornea, the procedure being repeated if necessary a third time, provided that the thickness of the cornea permits it It must be kept in mind that future operations may be necessary on the cornea under treatment, and therefore it is desirable to preserve as much as possible of the corneal thickness If the opacity invades only the outer third of the cornea only this portion should be excised .

# TREATMENT OF GLAUCOMA

PAUL A CHANDLER, M D

BOSTON

Many methods have been evolved for the treatment of glaucoma but there is considerable difference of opinion as to their selection and application. In this paper I shall briefly describe the procedures that my own experience has led me to employ in treating glaucoma of various types. The conclusions are drawn entirely from personal experience and are presented to invite discussion and comparison with the experience of others.

## ACUTE GLAUCOMA

Acute glaucoma may occur in some instances with practically no pain or congestion, whereas in others the pain may be violent and severe, with extreme congestion of the eye and even chemosis. Likewise, in instances of chronic glaucoma there may be congestion of various degrees. For purposes of treatment the two types—congestive and noncongestive—need not be differentiated.

Primary acute glaucoma, though much less common than the chronic form, is often so fulminating as to create one of the gravest ophthalmic emergencies. It is a distinct disease entity. The one characteristic which is invariably present is a shallow anterior chamber. If the chamber is normal or deep, one is almost certainly not dealing with primary acute glaucoma. Hemorrhagic glaucoma is sometimes first manifested as an acute attack, as is glaucoma rubrum. However, in these conditions the pupil is not widely dilated, the anterior chamber is usually normal or deep, the iris is greatly congested and a history of previous great loss of vision in the affected eye can usually be obtained. Exfoliation of the capsule of the lens may sometimes produce the picture of acute glaucoma with a deep chamber, as may a hypermature cataract or a subluxated lens. There are some eyes, apparently with a low margin of safety, in which iritis or uveitis may precipitate acute glaucoma. The differentiation of primary from secondary acute glaucoma is not always easy, because of the presence of severe corneal edema or bullous keratitis, yet it is of great importance to make it, so that the initial treatment, medical

or surgical, may be the proper one. Recently Dr David G Cogan, director of the Howe Laboratory of Ophthalmology at the Massachusetts Eye and Ear Infirmary, demonstrated the dramatic clearing of an edematous cornea by the instillation of 1 drop of ordinary glycerin. Practically all corneal edema except that with bullae will clear in less than ten seconds sufficiently so that one can study the back of the cornea, the aqueous and the iris with the slit lamp, and if the lens is reasonably clear one can usually see the fundus. It is almost the rule to find a few cells in the aqueous in acute congestive glaucoma. In many instances a great many cells are present, and there may even be pigmented synechias. Nevertheless, if the other classic signs and symptoms are present—shallow anterior chamber, semidilated pupil and acute fulminating onset—one is dealing with primary glaucoma and the eye should be treated accordingly. If, on the other hand, the anterior chamber is normal or deep, if there are extensive posterior synechias and especially if there are precipitates on the back of the cornea, the condition is surely secondary glaucoma. If there is cupping of the disk, the condition must be treated as chronic glaucoma and only a filtering operation will suffice. If the central vein is obstructed, the condition is hemorrhagic glaucoma and the situation is hopeless, except that in a few instances the eye may be saved by cyclo-diathermy. If the patient is diabetic and there is evident diabetic retinitis and dilatation of the vessels on the iris, a diagnosis of glaucoma rubrum is justified and the treatment is the same as that for hemorrhagic glaucoma.

If the condition is primary acute glaucoma, one must decide whether or not to operate and when to operate and one must choose the type of operation most likely to bring about permanent control of the tension. The important considerations are the duration of the attack and the visual acuity of the eye. Eyes vary tremendously in their vulnerability to high tension. Some eyes will tolerate high tension for days with relatively little damage to vision, while in others the visual acuity will go down in a few hours to an extremely low level. It is always preferable to lower the tension with a miotic before operating, if this is possible. The miotic

Read before the Section on Ophthalmology of the Michigan State Medical Society, October 1942, and before the Section on Ophthalmology, New York Academy of Medicine, Jan 17, 1944.



may be given every ten minutes for two hours, then every half-hour for two hours and every hour thereafter as long as it is used

How long should one try to reduce the tension by the use of miotics before resorting to surgical intervention? The factors which aid in this decision are the duration of the attack, the visual acuity of the eye and whether or not there is a substantial drop in the tension after two hours of miotic therapy. If the attack has been going on more than twenty-four hours, one should not defer operation more than five or six hours unless the tension is definitely falling. If the attack has been going on only a few hours, one may try miotics for as long as twelve hours if the visual acuity of the eye remains relatively good. No matter what the duration of the attack, if the vision is down to counting fingers at a few feet or less, surgical intervention should not be long delayed. In the treatment of a vulnerable eye in which the visual acuity has fallen to recognition of hand movements or less in a few hours, one should operate at once, without trying miotics at all. Five per cent neostigmine bromide combined with 20 per cent mecholyl chloride is probably the most effective miotic. One may use 4 per cent pilocarpine nitrate or 1 per cent physostigmine salicylate, or one may combine these drugs in various ways.

Assuming that the tension has been brought to normal with miotics, what further treatment should be employed? I believe that a single attack of acute glaucoma, except in extremely old people, calls for operation. Without operation almost invariably other attacks occur in spite of the regular use of a miotic, each taking some toll of the vision, until a final intractable attack occurs which may end disastrously for the eye in spite of an operation then performed. If one looks over hospital records of patients with acute glaucoma treated conservatively, one will often find a series of admissions before the final attack at which time even operation failed and all vision was lost. Acute glaucoma in old people may be treated more conservatively, for in these patients probably different factors are at work. If the tension is promptly lowered to normal with miotics, the regular use of fairly weak miotics will in most cases prevent further attacks. Even in old patients operation would be the treatment of choice were it not for its influence on the development of opacities in the lens.

If an operation is decided on, what is the operation of choice and when should it be done? If the tension cannot be brought down with miotics, paracentesis or posterior sclerotomy may be done as a preliminary measure. I seldom employ them. Of course iridectomy is the first

choice, but it must be realized that iridectomy, no matter how well performed, will not as a rule be sufficient in the treatment of acute glaucoma which has been neglected or wrongly diagnosed and treated with atropine. My own experience has led me to adopt the following general rules, though I fully realize that there are exceptions to these, as to all rules.

1 If the attack is less than forty-eight hours old, iridectomy is chosen whether or not the tension comes to normal preoperatively with miotics.

2 If the attack is forty-eight hours old or more, iridectomy is done if the tension comes fully to normal preoperatively and can be maintained there with reasonable use of miotics. In any case in which the tension can be brought to normal with miotics, surgical intervention is delayed while the use of miotics is continued until the eye is relatively free from congestion.

3 If the attack is forty-eight hours old or more and the tension cannot be brought to normal with miotics or, if brought there, cannot be maintained at the normal level without vigorous use of strong miotics, a filtering operation is chosen. Under these conditions it has been my experience that iridectomy only succeeds in changing the condition from acute to chronic glaucoma. When the eye quiets down after iridectomy, too often one finds the tension running from 30 to 40 mm (Schiotz). Trephining as the first operation for acute glaucoma has not shown good results as a rule. In the first place, with the tension high and the anterior chamber shallow there is always the danger of the lens coming forward and blocking the opening. Then, too often, a trephine opening in a congested eye closes within a short time. The operation most successful in my hands for glaucoma of this type is sclerectomy combined with iridencleisis. I would choose this first as the operation for neglected acute glaucoma.

It must be realized that even in the instances in which iridectomy alone is clearly indicated and properly performed there may occasionally be subsequent attacks of typical acute glaucoma, particularly if the original attack was noncongestive, which are disconcerting to both surgeon and patient. Fortunately these instances are rare, and subsequent attacks are usually controlled by continuous miotic therapy.

A few points about the technic of iridectomy are of importance. I used to think that any kind of iridectomy would suffice for the treatment of acute glaucoma, but experience has convinced me that success or failure may depend on the technic of the operation.

I remember in particular 2 cases of bilateral acute glaucoma, with the condition identical in the two eyes in each case. A properly performed iridectomy permanently relieved the tension in one eye, and a poor iridectomy done at the same time on the fellow eye failed to relieve the tension. The iridectomy should be broad and basal.

For anesthesia I usually make an orbital injection of 2 per cent solution of procaine hydrochloride with epinephrine (1:40,000) in the four quadrants, 1.5 to 2 cc in all, and wait ten minutes. If a general anesthetic seems advisable, pentothal sodium administered intravenously is satisfactory. I prefer a small sharp knife to a keratome. The incision is made without preparing a flap, since the latter is easily made with the knife. The incision made with a knife is finished more at right angles with the sclera than is an incision made with a keratome. There is therefore a tendency for the wound to gape, and the scleral bleeding, which is the most serious, always comes outside the eye. After the incision is finished, I wait without sponging until all bleeding has stopped before doing the iridectomy. This sometimes requires a considerable degree of patience, but it is well worth it, for then the only bleeding into the anterior chamber is that from the iris, which is never serious.

In treating a patient with acute glaucoma in one eye, one must be mindful of the danger of an acute attack in the other eye. Miotics should be used vigorously in the unaffected eye during the stay in the hospital. In fact, since acute glaucoma is apt to develop in the unaffected eye sooner or later, it is wise to continue indefinitely to use a miotic in it.

#### CHRONIC GLAUCOMA

When one first examines a patient who has chronic simple glaucoma, one measures the visual acuity and the tension and maps the visual field. These measurements indicate the status of the disease. One must then lay plans to maintain the patient's vision as long as he lives. Treatment will consist of the use of miotics or surgical intervention or both. Whatever the treatment, it must effectively prevent further reduction of the visual field. Unless the treatment accomplishes this, the diagnosis might just as well not have been made in the first place. To diagnose glaucoma and feel that one has done well in routinely prescribing 1 per cent pilocarpine nitrate to be used two or three times a day without ascertaining the effectiveness of this treatment is not to merit the confidence of the patient, to say the least. As the patient is observed over the weeks and months while receiving various treatments, one gradually gains more

knowledge of his particular condition and is able to form a better judgment as to the treatment and prognosis. I have found that it is often helpful at the outset to make tension studies over a period of three or four days. The patient is hospitalized, and the tension is taken four times daily, at approximately 8 a. m., 12 noon, 5 p. m. and 10 p. m.

The first day there is no treatment. The second day 1 per cent pilocarpine is used and the third day 2 per cent. In some cases the study is continued a day or two longer and 4 per cent pilocarpine nitrate or some other strong miotic is used. Such a study will often give an idea as to the type of glaucoma with which one is dealing, and one can use at the beginning of treatment the miotic which promises to be most effective in controlling the disease. The study may indicate at the outset that an operation must be done in order to hold the tension at reasonable levels. In such studies one observes several types of tension curves. There is a type in which the tension in the untreated eye never goes above the low twenties (fig 1). Miotics have no significant effect on tension in this type. There is a type in which the tension is usually low but is definitely elevated at some one period of the day. Miotics are often extremely effective against this type of glaucoma by eliminating the periodic elevations which are causing damage to the eye (fig 2). Then there is a type of glaucoma with relatively high tension in which strong miotics are usually required to maintain the tension at normal levels (fig 3), and another type with high tension in which even the strongest miotics are not effective (fig 4). Relatively advanced, so-called capsular glaucoma is usually characterized by high tension of the latter type.

In making the often difficult decision as to whether or not to operate such studies of tension are often exceedingly helpful. There are many other factors to be considered however. The behavior of the visual field over a period of time is, of course, the most important factor in the decision. The general health of the patient and his faithfulness in carrying out the recommended treatment must be considered. One must have regard as to whether the patient is easy-going and placid or a tense, nervous person on whom life imposes many stresses and strains. All other things being equal, one would be more inclined to operate early on persons of the latter than on persons of the former type. Perhaps the most important single factor is the age of the patient. I believe that few patients with an average life expectancy of twenty or thirty years can have glaucoma held in check over such a long period with miotics alone and therefore that

practically all patients under 60 years of age in good general health should have an operation For patients between 60 and 70 years of age, I believe an operation is indicated if extremely strong miotics are required to hold the tension

tion In treating such a patient, if the diagnosis is established early and there is a good visual field, one may be content to allow a slow loss under miotic therapy, whereas if the disease is already far advanced when the diagnosis is made,

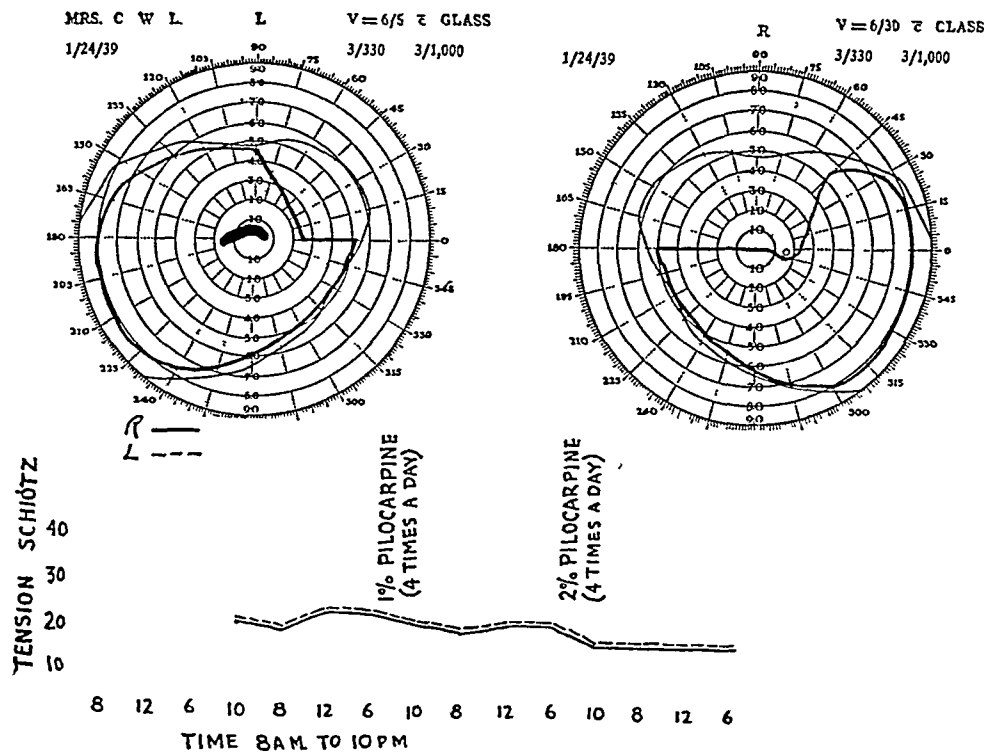


Fig 1—Visual fields and tension curve for a patient with chronic glaucoma with low tension

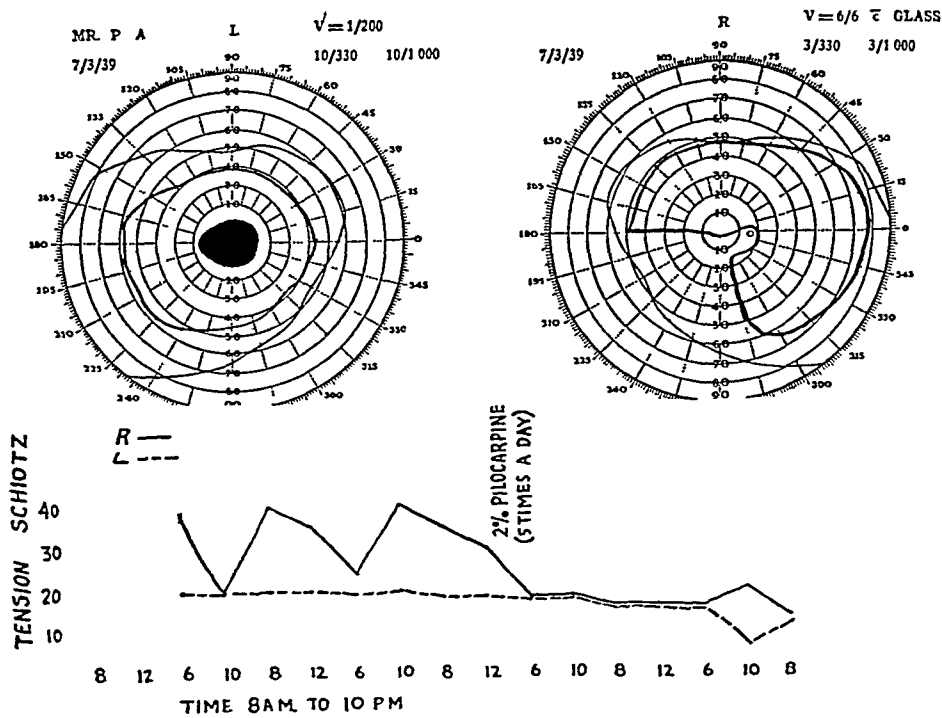


Fig 2—Visual fields and tension curve for a patient with chronic glaucoma with generally low tension elevated at one period of the day

at normal levels, for in such instances sooner or later miotics will no longer be effective It is in the treatment of patients over the age of 70 that it is often most difficult to decide the question of the desirability of surgical interven-

surgical intervention may be indicated at the outset, for the patient cannot afford to lose even a little In older patients I feel that a Schiötz tonometer reading in the thirties is an indication for operation, especially if there is rapid reduc-

tion of the field In all older patients, the indications for operation must be relatively stronger than in younger patients for any surgical procedure to relieve glaucoma in these patients almost invariably causes the development of opacities in the lens, or causes a definite increase in opacities already present It should be emphasized that in cases in which for one reason or another one wishes to avoid surgical intervention stronger miotics can be used at frequent intervals When a 1 or 2 per cent solution of pilocarpine nitrate used three or four times a day is ineffectual, a 4 per cent solution can be used as often as every two hours during the day

As to the type of operation to be employed each one of us must be guided by his own experience Let us employ the operation that we can perform most skillfully and that gives us the best results I favor trephining for most younger patients In my hands it is the most successful operation for holding down the tension for a long period I think it is particularly effective for eyes with relatively low tension The 1.5 mm trephine is used routinely, but in the treatment of juvenile glaucoma the 2 mm trephine is always used I definitely favor iridencleisis for all older patients, for I find that it seldom results in the hypotony so frequently seen after trephining under such conditions, and this means that it

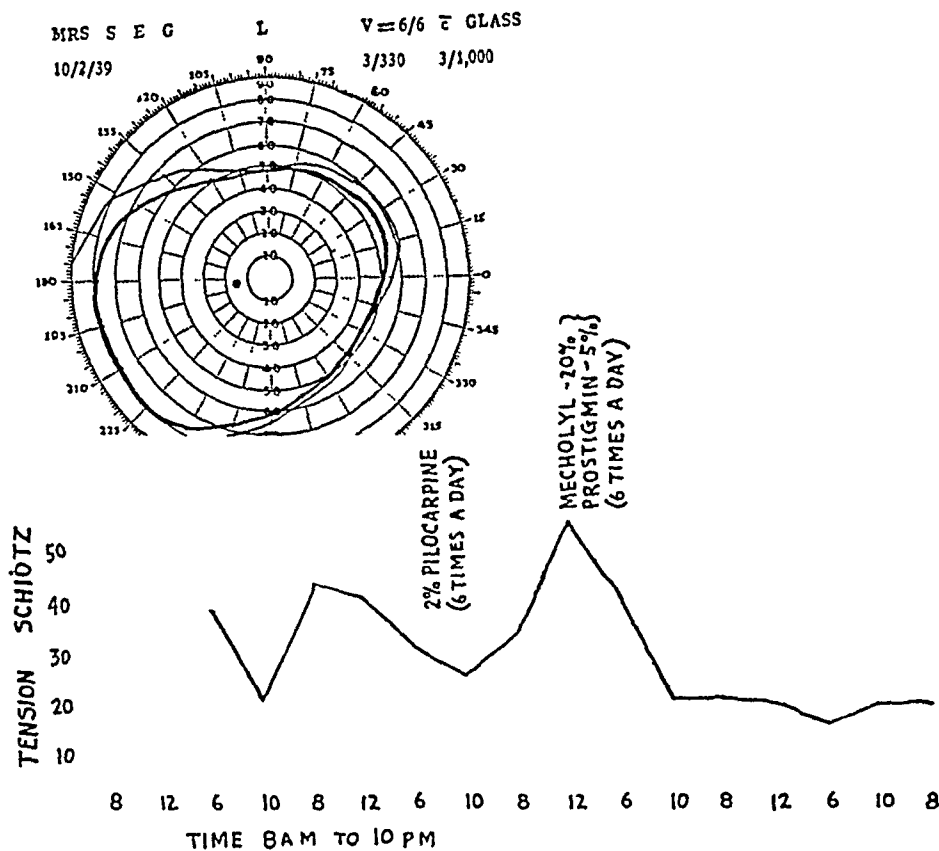


Fig 3—Visual field and tension curve for a patient with chronic glaucoma with relatively high tension which is controlled by strong miotics

In patients in the low tension group, in whom the tension is always under 25 mm (Schiøtz), miotics have little or no effect, but the loss of field is relatively slow I believe, therefore, that a patient 50 years of age with glaucoma of this type should have an operation but that for a patient of 65 or over an operation is practically never indicated

It is impossible to make fixed rules in regard to surgical intervention in chronic glaucoma, but in general it may be said that most of us have had many more occasions to regret not having resorted to an operation than we have had to regret operating Another fact to be remembered is that eyes with early glaucoma as a rule do much better after surgical intervention than those in which the disease is advanced

is much less apt to cause cataract In general, I favor an iris inclusion operation for eyes which must be operated on in the presence of a relatively high tension Under these conditions after a well executed trephination I have seen the lens come forward and block the opening, completely nullifying the operation Iridencleisis combined with sclerectomy is my operation of choice for congested eyes, as it offers the best chance for permanent filtration Also, when I perform an iris inclusion operation for a younger patient, a sclerectomy is done I treat glaucoma due to exfoliation of the capsule of the lens no differently from glaucoma in which exfoliation is not present I believe that the iris inclusion operation with sclerectomy is better than trephining for such a condition, since I have several times

seen a perfectly functioning trephine opening close within a year or two after the operation

As to the technic of the iris inclusion operation, one may of course use either a keratome or a knife for the incision. An incision made with a keratome probably offers the least trauma to the eye, but if the anterior chamber is excessively shallow it requires a good deal of skill to make it properly. One may prepare the flap beforehand as in the trephining operation, or one may make the flap with the knife, or if the keratome is used the Reese type of incision may be made. My own preference is to use the knife for the incision, as in iridectomy, without previous preparation of the flap. With a little care one can

When this is done, the forceps is released and the iris is not touched again. Under certain circumstances a tongue of iris is prepared and the sphincter is left intact. No attempt is made to rearrange or flatten the tongue of iris. Any such manipulation may further traumatize the pigment epithelium, which must remain more or less intact in order that a proper filtering scar may develop. Atropine is used postoperatively, not as a routine but according to the amount of reaction, the size of the pupil and the amount of blood in the anterior chamber. In some instances no atropine is used at all. When sclerectomy is combined with iris inclusion, after the incision is finished the conjunctiva is sepa-

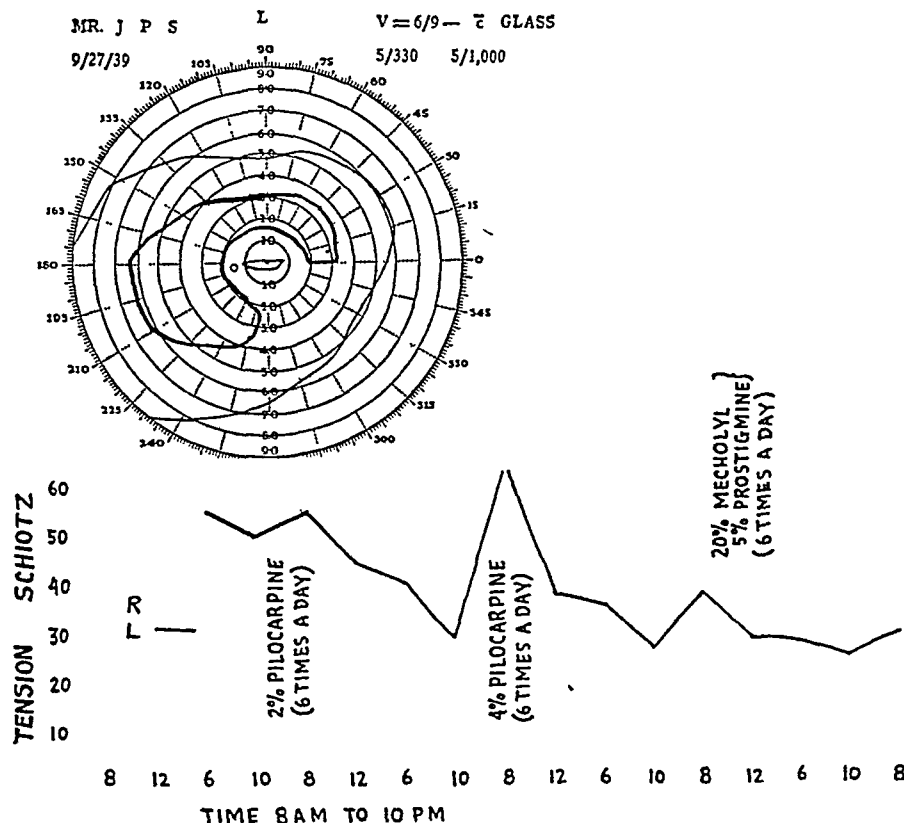


Fig 4—Visual field and tension curve for a patient with chronic glaucoma with high tension which is not controlled by strong miotics

make with the knife as large a conjunctival flap as necessary. It has seemed to me that this caused less trauma to the conjunctiva than if the flap were prepared beforehand, and there is better visibility in making the incision. As in iridectomy in which the incision is made with a knife all blood from the wound invariably escapes on the outside of the eye rather than into the anterior chamber. After the incision is finished I like to wait without sponging until the scleral bleeding has stopped. If one continually sponges, the blood may be forced into the anterior chamber. The iris should be withdrawn with great care, so as to avoid unnecessary trauma to the pigment epithelium. I usually cut the sphincter on each side of the forceps

rated from the anterior scleral lip by gentle dissection with the tip of a keratome and then a piece of the sclera is bitten off with a Holth or a Berens punch

Chronic glaucoma coexisting with immature cataract is a particular problem. Treatment depends on the extent of the cataract and on the severity of the glaucoma. Miotic therapy, if it is reasonably effective in controlling the glaucoma, is always preferable until the cataract has advanced sufficiently to warrant its removal. Unfortunately, if the opacities in the lens are central, the miosis may diminish central vision to an extent that is incapacitating to the patient. If the vision is cut down to 20/50 or less by the opacities in the lens, intracapsular extraction with

a broad basal iridectomy will often control the glaucoma. In instances in which the tension remains too high after such an operation, miotic therapy, perhaps combined with the use of 1 or 2 per cent epinephrine, will usually be effective. In rare instances further surgical intervention, preferably cyclodialysis, will be necessary.

If central vision is 20/40 or better without miotics and miotics reduce the vision below 20/40, I believe that broad iridectomy followed by miotic therapy is preferable to immediate extraction of the cataract. Of course a filtering operation would be expected to afford better control of the tension in such cases, but if performed on an eye with already well developed opacities in the lens it almost invariably causes a rapid increase in the opacities. To be sure, if the cataract develops rapidly, extraction of the lens can be done, but the operation is undoubtedly more difficult to perform on such an eye. After iridectomy, on the other hand, if extraction of the lens becomes necessary, it is simplified by the previously performed iridectomy.

When any operation designed to produce a filtering scar is done, it is extremely important to keep the patient under close observation during the first few weeks after the operation. In some instances there is nothing to be done, but in others early "massage"<sup>1</sup> of the eye may make the difference between success and failure. By using the proper amount of "massage," the tension may finally become stabilized at the desired level. In some instances if one waits as long as two weeks after operation before beginning pressure on the eye it may be too late. I like to see the patient at least once a week during the first six weeks after the operation.

#### BUPHTHALMOS

For the treatment of buphtalmos or infantile glaucoma iridencleisis has proved more successful in my hands than trephining. In any operation for glaucoma of this type it is of the greatest importance that adequate massage be carried out by the parents after the child leaves the hospital. In fact, I believe that the after-care by the parents is so important that the operation is almost certain to fail without it. On the other hand, if firm pressure is made on the eyes four times a day, day after day without fail, one can anticipate a much higher percentage of success than is generally realized. One must take the parents into one's confidence and carefully explain the nature of the disease and the principle of the operation. They must be made to understand that their

† role is as important as that of the surgeon, that

they must do their part if the disease is to be controlled. There is usually hypotony for one to two weeks after the operation. Pressure on the eye is begun as soon as the tension rises to normal. Barkan's operation of goniotomy for this type of glaucoma sounds promising, I have had no experience with it.

In the general management of patients with primary glaucoma, I feel it my duty to remind them by letter or telephone when it is time for them to be seen and to continue to do this until they come to the office or I am assured they are under the care of another oculist. Patients being treated with miotics in whom the tension seems to be under control are seen three times a year. After successful surgical intervention they are seen twice a year. Of course any unusual elevation of tension calls for more frequent visits until it can be ascertained that the revised treatment promises to hold the tension within normal limits.

#### SECONDARY GLAUCOMA

If it is difficult to lay down rules for the treatment of primary glaucoma, it is well nigh impossible to do so for the treatment of secondary glaucoma, every instance of which presents its own peculiar problem. The only general rule which can be made is that in the treatment of secondary glaucoma one should employ conservative measures as long as possible.

In the treatment of glaucoma secondary to acute iritis I always continue the use of mydriatics. The first move is to use 1 or 2 per cent solution of epinephrine bitartrate three or four times a day. If this fails, paracentesis is tried, and if paracentesis holds the tension down for only a few hours, I try a Reese incision<sup>2</sup>.

With uveitis, a more chronic disease, Reese incision, repeated as often as necessary, will

<sup>2</sup> For combating secondary glaucoma an incision without iridectomy was introduced by Verhoeff at the Massachusetts Eye and Ear Infirmary many years ago. He termed it the "Reese incision" because it was similar to the incision made by Robert Reese in performing iridectomy. Whether Reese himself ever employed it without iridectomy, I do not know. The incision is made subconjunctivally, usually from above, with a keratome, and it produces an exceedingly small cut in the conjunctiva far from the scleral incision. Previously Verhoeff had made the same sort of incision by means of a Ziegler knife-needle. The tip of the keratome is engaged in the conjunctiva 7 or 8 mm from the limbus and passed subconjunctivally to a point about 1.5 mm from the limbus and then into the anterior chamber. The incision into the anterior chamber is usually 6 to 7 mm broad. No suture is used. Pressure on the eye is begun the following day and repeated several times daily, usually by the patient himself. Each time pressure is used it must be applied continuously until the eye is soft. The incision may thus be kept draining for days, sometimes for weeks.

<sup>1</sup> By "massage" is meant firm, steady pressure on the eyeball.

often tide over a difficult situation. A year or two ago, in treating a patient with bilateral uveitis with secondary glaucoma, five Reese incisions were made in each eye over a period of a few months. In the end the uveitis quieted down, the tension remained normal, the vision in each eye was 20/20 and the visual fields were full. In the treatment of a subsequent attack of uveitis lasting several months a single Reese incision in each eye was sufficient to control the tension, since the patient was by that time so well trained in massage that he never allowed the incisions to close. In the treatment of intractable secondary glaucoma, such as that in sympathetic uveitis, if the Reese incision proves ineffective I have occasionally used iridencleisis with sclerectomy successfully.

In the treatment of glaucoma due to iris bombé I favor iridectomy rather than transfixion of the iris, for the slitlike opening produced by transfixion will not infrequently become closed by hemorrhage or exudate. When iris bombé is present without increased tension, it is wise to defer operation until there is elevation of tension. In some eyes with iris bombé the tension may remain normal or even subnormal, possibly owing to atrophy of the ciliary body. Iridectomy on such eyes will often result in atrophía bulbi and should not be done unless the eye is practically blind as a result of closure of the pupil and the presence of opacities in the lens. In such circumstances iridectomy may be combined with extraction of the lens in a final attempt to obtain vision, for the situation is such that there is nothing to lose and possibly something to gain by operating.

Glaucoma following dissection of the intact lens or following traumatic cataract calls for prompt linear extraction of the lens. Increased tension after incomplete removal of the lens is probably best treated by repeated paracentesis. The tension usually subsides as the lenticular matter is absorbed.

Hypermature cataract often causes acute glaucoma. Some oculists favor iridectomy in the treatment of this condition, followed by extraction of the lens at a later date. Whether or not the tension can be brought to normal with miotics preoperatively, I much prefer extraction of the lens with broad iridectomy as the first operation. I believe one runs an unnecessary additional risk in doing a preliminary iridectomy. Following preliminary iridectomy for acute glaucoma due to hypermature cataract there may be serious bleeding into the anterior chamber or persistence of a flat or shallow chamber, with return of the glaucoma and persistent congestion, making an extremely complicated situation.

After severe contusion of an eye the anterior chamber is sometimes black with blood and the pressure within the eye elevated. There is no visible structure to the clot, and the cornea resembles a section of a black marble. Since such a clot will never absorb in time to save the eye, an operation should be done at once. Aside from the possibility of damage from the glaucoma, hematogenous pigmentation of the cornea will begin sometimes within thirty-six hours. An incision should be made with a keratome and the blood clot should be washed out of the anterior chamber.

The situation is quite different, however, if one can see structure to the clot or if any portion of the iris is visible. In such conditions the blood is usually absorbed rapidly, and the eye should be left alone if the tension is normal or only slightly elevated. A considerable elevation of tension can often be successfully combated with miotics, but if it cannot be controlled paracentesis should be done. When the blood is absorbed and the tension is normal, the use of a miotic can be discontinued and a mydriatic employed for the remainder of the period of convalescence. During the first few days of treatment the use of hot compresses should be avoided, for their employment undoubtedly favors continued bleeding.

Subluxation or complete dislocation of the lens may cause glaucoma. When the lens becomes dislocated into the anterior chamber, it usually causes acute glaucoma and must be removed without delay. Increased tension due to partial subluxation of the lens backward, from trauma, sometimes proves to be transient and can be successfully controlled with miotics. If the tension is uncontrolled, however, the lens should be removed. When the lens is completely dislocated into the posterior chamber, it is sometimes well tolerated without any elevation of tension, under these circumstances it is best left alone. If intractable glaucoma ensues, however, the lens should be removed if possible. Removal of a subluxated or completely dislocated lens is a formidable procedure and should not be undertaken without strong provocation.

The glaucoma that sometimes occurs after uncomplicated extraction of a cataract and especially after needling of a secondary membrane constitutes a difficult problem. In a few instances the condition is controlled by miotics alone, and the combined use of a miotic and 1 or 2 per cent epinephrine is particularly helpful. For operative treatment I continue to employ cyclodialysis, but I must confess that in my hands it is not always effective. When cyclodialysis fails, trephining with the 2 mm blade will not infrequently be



successful As a last resort cyclodiathermy may be tried, but only as a last resort, for I consider it to be heroic treatment If cyclodiathermy is extensive enough to control the tension, it sometimes leads to atrophy bulbi

A general rule for the surgical treatment of secondary glaucoma is to use all the conservatism consistent with maintaining the vision of the eye Never employ a big operation if a minor one may tide things over

One grows in wisdom in treating glaucoma only by continually inquiring into the causes of failures If one form of treatment fails to relieve glaucoma of a given type another should be tried the next time the same condition is encountered Let us not continue to make the same mistake over and over again The treatment of glaucoma is one of the major problems of ophthalmology and requires the employment of the ophthalmologist's best judgment and skill

5 Bay State Road

#### DISCUSSION AT MEETING OF NEW YORK ACADEMY OF MEDICINE

DR ARNOLD KNAPP, New York We know that Dr Chandler has been particularly interested in surgical treatment of glaucoma, and we are glad that he has taken the trouble to give us the benefit of his experience and careful observation There are a great many questions we should like to ask him, but I am going to speak of only one or two of them

First, I was particularly interested in his being able to accomplish something in the treatment of buphthalmos by means of pressure My results in the treatment of buphthalmos have been bad Frequently the patients disappear from observation and no one knows what the final results are

Second, in speaking of operations for acute glaucoma, Dr Chandler mentioned a case in which the formation of a perfect coloboma gave a good result and a poor iridectomy failed to relieve the tension In my experience it is not always possible to obtain a clean coloboma in an eye with acute glaucoma, because the iris is too friable, and an imperfect coloboma often gives a surprisingly good result

In discussing surgical treatment of hypermature cataracts that cause glaucoma Dr Chandler said that the cataract should be extracted immediately, which is an interesting observation I have always tried to get the eye in a better condition by an iridectomy and then, after about three weeks, extracted the cataract in the capsule

I noted that Dr Chandler is partial to iridencleisis among the decompression operations for chronic glaucoma This reminds me of what Dr John Weeks always used to say "Do whatever operation you have confidence in"

DR MARK J SCHOENBERG, New York We are all much obliged to Dr Chandler for his fine paper, especially for the emphasis he placed on the importance of proper technic and for his discussion of the indications for the various operations for glaucoma The details he mentioned concerning the after-treatment are certainly welcome, and I agree with him entirely that so-called minor details are apt to determine whether the outcome of an operation is a success or a failure

May I mention one more point which is of equal importance? This is the avoidance of surgical trauma It is one thing to know the technic and an entirely different thing to be gentle in assaulting the tissues with surgical implements Much of the "roughness" of some surgeons may be due to insufficient training or to a state of tension, but some of it is due to the fact that teachers are not putting sufficient emphasis on the importance of gentleness in handling the tissues

If eyes come out of the operative ordeal without much inflammatory reaction, they owe this not only to the patient's vitality but often mostly to the gentleness of touch of the man who performed the operation

DR JOHN McLEAN, New York I should like to thank Dr Chandler for his practical and instructive talk and to add a few questions I noticed that he was inclined to stress the combination of cataract and glaucoma, and I should like to ask how he handles the extraction of the cataract after a successful filtering operation That sometimes can be an important point The converse, which I do not think he mentioned, occurs when a typical aphakic glaucoma develops apparently as a result of an operation for cataract which has gone along rather smoothly except for delayed reformation of the anterior chamber What is the best approach under these circumstances? Some of us are enthusiastic about cyclodialysis and believe that this is the only condition for which cyclodialysis has a real value

Dr Chandler spoke about the danger of expulsive hemorrhage in operations on eyes which are hard, especially in extraction of a cataract I wonder what he thinks about the use of retrobulbar injections, particularly of sizable amounts of epinephrine, as a means of reducing the tension, possibly combined with massage before opening the eye to help reduce the possibility of hemorrhage

Finally, I noticed that Dr Chandler prefers an incision made with a knife in the Lagrange operation because he can make a more perpendicular cut at the limbus with a knife than with a keratome I wonder whether he has any particular reason for not using the so-called "scratch" or ab externo incision, which can be made perpendicularly



DR PAUL CHANDLER, Boston In regard to buphthalmos, which Dr Knapp mentioned, I would say that to my knowledge I never cured a patient with that disease until the last 3 were treated by the "pressure" method. The parents of the 3 children were extremely cooperative and were well instructed beforehand. I think the eyes are still holding. The first patient has been followed for three years, the second for eighteen months and the third for nine months. The corneas have not enlarged, and the pressure has remained normal.

A poorly performed iridectomy may sometimes work better than a well performed one, especially if a tab of iris is left in the wound and a filtering scar develops.

In the treatment of hypermature cataract and acute glaucoma, I was taught to do an iridectomy. I have seen several eyes with this combination of conditions which had copious bleeding into the chamber after the iridectomy, but, although I have not encountered many of them, I have never had any difficulty in extracting the lens as the first operation.

I agree that trauma in surgical procedures should be avoided as far as possible. In doing a trephining I think it is better not even to sponge, but to wash away the blood by irrigation when splitting the cornea. In iridencleisis it is of the greatest importance that the iris be grasped with extreme gentleness when it is withdrawn. One or more cuts may be made, according to the preference of the surgeon, but then the iris should be released and not touched again. I make no attempt to flatten or smooth it, because if the pigment epithelium is damaged a filtering scar will not develop.

Extracting a lens in the presence of an adequate filtering scar is not an easy operation, particularly if there is a large bleb encroaching on the cornea. This condition sometimes occurs following tre-

phining. Such eyes do not require any flap. I usually cut the conjunctiva loose on either side of the bleb and put in so-called corneoscleral track sutures, which under these circumstances should be largely corneal, and then make a small corneal incision. If the sutures are largely corneal it is easier to make the section than if they are placed in the usual fashion. The tracks are then rethreaded. The lens is usually tumbled, since the larger scleral lip makes it more difficult to grasp the lens above. The capsules are usually fairly strong. The corneoscleral suture gives a satisfactory closure of the wound.

I think that glaucoma in aphakic eyes is probably the most difficult to deal with. Fortunately in a few eyes with this condition the tension can be lowered by the use of miotics plus the use of 1 per cent epinephrine once or twice a day. If this fails, I choose cyclodialysis as the first operation, as Dr McLean said he did. Either I do not do this skilfully or my luck has been bad, for I have not had the best of success with it. If this treatment fails, I like to do a 2 mm trephining instead of repeating the cyclodialysis. Then pressure on the eye will often cause a small localized bleb to develop with a satisfactory result. It might seem that the vitreous would get into the trephine hole when this operation is done, but it is surprising how seldom that occurs.

I agree that pressure on the eye is helpful in conjunction with retrobulbar injection when the lens is extracted from a hard eye. I use retrobulbar injection in every intraocular operation, and I like to wait five or ten minutes after the injection is given before operating. In handling hard eyes I maintain firm pressure on the eye all the time I am waiting for the anesthetic to take effect. Sometimes hard eyes will soften surprisingly during that period.

# INDUSTRIAL INJURIES OF THE EYE

ELBERT S. SHERMAN, M.D.

NEWARK, N. J.

The treatment, including operative procedures, of industrial injuries of the eye does not differ materially from that of nonindustrial injuries, but because of the workmen's compensation laws, certain factors other than treatment enter into their management.

Compensation for "personal injury to an employee by accident arising out of and in the course of his employment" is the phraseology used in these laws, which since 1911 have been almost universally adopted in this country. Thus, with few exceptions, every case of industrial injury is what is commonly termed a compensation case. It may also become a litigation case.

I do not want to pose as an industrial ophthalmologist, but having practiced ophthalmology for many years in the center of a large industrial area in which there is a great variety of industries, I have had a considerable number of patients with injuries of the eye sent to my office. Because of the great acceleration of industrial activity during the past two or three years, there has been a great increase in the volume of this class of work.

Employers and insurance companies have gradually learned by expensive experience that it pays to have ocular injuries, even apparently trivial ones, taken care of by an ophthalmic surgeon, preferably one familiar with compensation work. They are willing to pay well for honest, competent service. The president of one of the large insurance companies said <sup>1</sup>

The modern insurance company no longer considers it economy to organize its staff of surgeons on the basis of low fees. There is a sincere desire to give the industrially injured the highest grade of surgical care that can be secured.

Injuries to the eye are the most expensive type of industrial accidents.

Compensation includes (1) the cost of hospitalization and surgical care, (2) pay for temporary disability (loss of time) and (3) pay for permanent disability (impairment or loss of

function). Permanent disability may be partial or total. In the case of an injury to the eye, after treatment has ended and a necessary period of observation has elapsed, the ophthalmic surgeon is asked to give an estimate of the permanent disability, if any. If there is no loss of visual function, or if visual acuity is reduced below the arbitrary point of industrial blindness, which is usually 20/200 but varies in different states, the estimate is easily made. However, an estimate of no permanent disability is sometimes disputed by the employee, who has now become what is known in compensation court parlance as the petitioner. By this time, and often much earlier, he has a lawyer, who hires, for a contingent fee, a more friendly expert on the eye. Then, if a satisfactory settlement cannot be effected with the employer, who is now termed the respondent, all parties must appear in the compensation court.

Computation of the percentage of loss of vision in cases of partial permanent disability is often more difficult and requires, besides good diagnostic ability, a knowledge of the standard method of evaluation of industrial visual disabilities approved a few years ago by the American Medical Association, or some modification of this method acceptable in the state in which one practices. This phase of the subject has been discussed so well and authoritatively by Snell <sup>2</sup> that further reference is unnecessary. Fortunately, in all but a small percentage of cases, the injury is trivial, and the question of compensation does not come up.

I am aware that compensation work is distasteful to, and is shunned by, some ophthalmologists. This is not surprising in view of newspaper reports of practices revealed in New York by the recent investigation of abuses of workmen's compensation laws, in which it was charged that 3,000 physicians received \$5,000,000 in "kickbacks" last year. However, I know of no more useful or satisfactory work than the care of industrial injuries of the eye, particularly now, when the conservation of man hours and sight is so important to the war effort,

Read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, Dec 20, 1943.

<sup>1</sup> Burns, F. H. Paper presented at the meeting of the Board on Traumatic Surgery of the American College of Surgeons, 1928.

<sup>2</sup> Snell, A. C., Sr. A Treatise on Medicolegal Ophthalmology, St. Louis, C. V. Mosby Company, 1940.

and it is regrettable that some good ophthalmologists fear to risk the smearing of their reputations by taking cases of this kind. In New Jersey, I believe, there are few such abuses, at least among the ophthalmologists. There is no reason that industrial injuries of the eye cannot be handled as honestly as any other kind.

Another feature of industrial work that is objectionable to some physicians is the necessity of making reports. When an employee is disabled by injury, the employer or his insurance carrier pays him a fixed percentage of his wages while he is unable to work. If there is some degree of permanent disability, the payments are continued for a specified time, the length of which depends on the nature and extent of the disability. In making these payments and in determining when they shall cease, the insurance companies depend almost entirely on the reports of the surgeon, and in the absence of this authority payment to the injured workman is often delayed. The Workmen's Compensation Bureau will not make any award for permanent disability without a physician's report. Reports are, therefore, essential. If one has a considerable number of cases of industrial ocular injuries, the work can readily be organized so that the reports are made quickly and almost automatically. My associates and I have most of them taken care of by the nurse or her assistant. We have found it necessary, for several reasons, to have waiting and treatment rooms separate from those used for other patients. To physicians who are not familiar with them, the usual forms for report of accidents used by the casualty companies may look formidable, but for slight injuries of the eye, which include the large majority of accidents involving the eye, only three or four essential questions need be answered. Several years ago I made a short form for the report of injuries of the eye, which has been a great time saver. On it are spaces for the name of the workman, whether he is to return for further treatment, the diagnosis and an estimate (actual or tentative) of temporary or permanent disability. For most cases this gives all the information needed or desired. It is given to the workman in a sealed envelope to be taken to his employer, who, if he is not self insured, forwards it to his insurance carrier with his accident report.

When there is likely to be permanent disability, a final report should not be made until function has been restored as fully as possible. In most cases it is evident at once that there will be no disability. In a few cases it can be seen, from the nature and extent of the injury, that total loss of vision is certain. In other

cases, after the acute symptoms have subsided, sufficient time should elapse for the gradual improvement which often occurs, and may continue over a period of months, or for the development of sequelae, before a final report is made. This applies particularly to corneal injuries, uveitis, opacities in the lens and vitreous, partial optic nerve atrophy, paralysis of the ocular muscles, both external and internal, and certain lesions of the fundus. While one should be cautious in making a prognosis, astonishing improvement often occurs in the impairment of vision caused by serpiginous and other traumatic ulcers, or in the astigmatism resulting from nonpenetrating wounds of the cornea and some other conditions. This is also true of traumatic paralyzes of the extraocular muscles. The diplopia often clears up completely in from six months to a year. Fortunately, in compensation work, the surgeon may usually keep the patient under observation as long as necessary. He should not permit himself to be hurried into making a final report prematurely. The period of observation may sometimes last for many months after the patient has returned to work.

In industrial work an accurate history of the accident is important. This may be brief or more extended, depending on the nature of the injury. Most industrial injuries of the eye are trivial and recover with no permanent impairment of vision or loss of time, but every case has the elements of a potential claim. Therefore, when the patient is first seen, as a matter of justice both to the employer and to the employee, a record should be made of when, where and how the accident occurred, of previous injuries, of the vision of both eyes, and of any preexisting pathologic changes, such as scars on the cornea or opacities of the lens. Not infrequently, sometimes months after a slight injury, an employee will, often in good faith, falsely attribute to it a serious loss of vision, which is really due to a preexisting condition. It has been shown that such defects are present in 20 per cent of workmen.<sup>3</sup> Unjust claims of this kind cost insurance companies and employers large sums of money. If an adequate examination and record have not been made, it is sometimes impossible to defeat such a claim. Because of the nature of the case, it is not always possible to make an accurate visual test of a recently injured eye, but this should be done as soon as conditions permit. Simulated amblyopia seldom appears until the employee has had time to reflect on the possibilities of capitalizing

3 McAuliff, G. R. Noncompensable Visual Defects in Industrial Ophthalmology, *Am J Ophth* 11 714 (Sept) 1928

on his accident. If the impairment of vision is not satisfactorily accounted for by the recent injury, the real cause should be ascertained.

Several years ago, Zimmer,<sup>4</sup> director of the Division of Workmen's Compensation, Department of Labor of New York, in a paper read before this section, commented on the importance of records. He said

The department is constantly pointing out to doctors the necessity of making and retaining complete case records. Experience has taught that record keeping is even more necessary in eye cases than in most other forms of injury. Many physicians seem reluctant to answer the all-important question as to whether the injury has produced loss of vision. It should hardly be necessary to point out that the reports should include visual tests and a pathologic description of the uninjured eye. These data are of grave importance in many cases in which the issue is one of activation or precipitation of a dormant disease. It is likewise frequently important for comparative purposes in measuring the visual loss of the injured eye. Any one, whether layman or physician, familiar with the history of cases in compensation procedure will agree that this matter of accurate and complete records cannot be overemphasized.

Sound judgment is not always used in correlating a traumatic lesion of the eye with its claimed results. If the alleged visual disability of a workman with an incentive for deceiving the examiner is not accounted for by ocular changes, as revealed by an adequate examination, the estimate of the amount of disability should be based on what is reasonably in accord with the physical findings. For instance, a small superficial scar of the cornea, which in the light of one's experience cannot, because of its size and location, cause more than 5 or 10 per cent impairment of vision, should not be rated as producing a 50 per cent loss simply because vision is apparently reduced to 20/100. Neither should impairment of vision caused by such conditions as a cataract which is clearly senile, lesions of the fundus due to general disease, old opacities of the cornea or amblyopia due to squint or anisometropia, be charged to a recent injury of the eye simply because the claimant insists that the eye was "all right" before the accident occurred. Yet such claims are being made constantly and, if supported by medical testimony sufficient to raise a slight doubt in their favor, are often successful. Too often the medical opinion in these cases is based not on probabilities but on remote (or imaginary) possibilities. The medical expert's fee for giving his opinion, or testimony, in court should not be contingent on the successful outcome of the case for the side which he is representing.

Reports of ocular injuries should be concise and the terminology as simple as possible. When writing them, one should remember that they are to be read by laymen. Terms like "O. D." and "O. S." are usually puzzling to the reader. It is just as easy to say "right eye" and "left eye." The same applies to "R. V." and "L. V." If it is necessary to use such terms as ptosis, iridodialysis, aphakia, hyperopia or myopia, which are unfamiliar to the laymen, their meaning expressed in simpler words, in parentheses, should follow.

When, as frequently occurs, an insurance company requests an examination of and opinion concerning an eye that was injured months previously, it is usually interested in one or more of three or four items: (1) the nature and evaluation of the disability, (2) any causal relation between the present condition of the eye and the accident of a given date, (3) indications for further treatment and (4) the prognosis.

Evaluation of the disability is often complicated by the presence of a preexisting or non-compensable defect. It is then often difficult, or impossible, to estimate what percentage of the disability or visual loss is the result of the recent accident. If the patient is seen soon after the accident, old defects are usually recognized as such and noted, but when he is referred months later, the difficulties may be great. The picture is commonly confused by such preexisting conditions as chronic conjunctivitis, scars on the cornea, old adhesions of the iris, opacities on the lens, glaucoma and presbyopia. Often it is vigorously claimed by the examinee that the eye was all right before the accident. The workman is usually given the benefit of any doubt that cannot be resolved.

One occasionally has a case that involves the compensation law doctrine of acceleration or aggravation of a preexisting disease. I refer particularly to those instances of apparently trivial injury, such as a foreign body in the cornea or a slight abrasion, which is followed by gross inflammatory changes in the eye, out of proportion to the severity of the trauma. The uveal tract is most often affected, less frequently the cornea. The more common manifestations are iritis, iridocyclitis, acute choroiditis and persistent ulceration of the cornea, and occasionally there is interstitial keratitis. I believe that the most usual underlying cause is focal infection. Sometimes the source of the infection is in the tonsils or the prostate, but more often, in my experience, it is about the roots of the teeth. When the focus is found and removed, the improvement in the ocular condition is often strikingly prompt and rapid.

<sup>4</sup> Zimmer, V. A. Workmen's Compensation Problems, Arch. Ophth. 7:367 (March) 1932.

Other causes are syphilis and tuberculosis. A few years ago, in discussing a paper on post-traumatic ocular tuberculosis at a meeting of the American Academy of Ophthalmology and Oto-Laryngology, Edward Jackson said "We have only learned within relatively few years the effects of trauma in producing outbreaks of interstitial keratitis." He expressed the certainty that he had seen several cases of this condition resulting from slight injury of the cornea. We have had 2 or 3 such cases. In 1 case a man aged 23 had had a foreign body removed from the cornea of the right eye three days previously. The eye was slightly red, and there was a faint, deep haze in the lower half of the cornea. This process progressed rapidly. Four days later there was typical interstitial keratitis, with the usual uveitis. Two weeks after the date of the injury the left eye became similarly affected. The man had Hutchinson teeth and a 4 plus Wassermann reaction of the blood. When claim is made for compensation in such cases, the courts have held the employer responsible for the treatment and disability of both eyes.

With regard to the doctrine of aggravation, in the paper to which I have referred, Mr. Zimmer stated:

Under the theory of compensation principles, firmly fixed by court interpretation in this state, traumatic aggravation or precipitation of a latent condition is the equivalent of causation. Under this theory there are presented to the department a very large number of cases in which one must determine whether and to what extent the injury incited the onroad or development of the diseases which in themselves are capable of reducing or destroying vision. A few of the more important examples include glaucoma, latent tuberculous conditions and syphilis. The latter cases present extremely difficult problems, and in connection with them there arises a great deal of medical controversy.

Sometimes a workman who is sent for treatment of an inflamed eye will say there was a foreign body in the eye a few days before, but, when questioned, he can fix no particular time when the alleged accident occurred and may admit that he thought there was something in the eye because it was uncomfortable. If the case is clearly not compensable, especially if the injury is serious, the facts should be reported to the employer (or the insurance carrier), so that he may have the choice of authorizing or refusing further medical care.

671 Broad Street

# LIPEMIA RETINALIS IN THE NONDIABETIC PATIENT

CECIL W LEPARD, M D

DETROIT

Since certain changes in the appearance of the arteries and the veins of the retina were described by Heyl<sup>1</sup> as lipemia retinalis in 1880, various other authors have reported in detail some 50 cases up to the present time and thus have made lipemia retinalis well known to the ophthalmologist. Records from larger clinics and hospitals indicate that it is more commonly observed than reported in the literature. With the exception of Wagener's case,<sup>2</sup> reported in 1922, the condition has been observed entirely in patients with diabetes. This has led authors of textbooks to give the reader the impression that diabetes is the only disease wherein this phenomenon may be seen in the fundus.

The level of blood lipids at which lipemia retinalis is first recognized and the level at which it disappears have been carefully determined by several authors (Chase,<sup>3</sup> Kollner,<sup>4</sup> Parker and Culler,<sup>5</sup> McKee and Rabinowitch<sup>6</sup> and Lepard<sup>7</sup>). Although there is some variation in these levels as determined by the different authors, lipemia retinalis appears approximately when blood fats increase to above 3.5 per cent and disappears when these fats decrease to below 2.5 per cent.

Hardy<sup>8</sup> stated the belief that the occurrence of lipemia retinalis is of bad prognosis. However, later it was found that patients with this condition have the same expectancy as patients with severe diabetes. In a series of 38 cases, Parker and Culler<sup>5</sup> noted that acidosis was present in all but 2 patients. Marble and Smith<sup>9</sup> stated that lipemia retinalis occurs usually, if not

exclusively, in patients with acidosis or in persons who have recently had acidosis.

Lipemia retinalis was observed over a period of several years in an otherwise well person showing a persistent high concentration of fats in the blood. Complete studies on the blood were made and component lipids of plasma and erythrocytes determined. Other clinical and metabolic studies were made by Bernstein, Williams, Hummel, Shepherd and Erickson.<sup>10</sup> From the results of these some of the questionable phases of lipemia retinalis may be studied, and a correlation between the ophthalmoscopic findings and the components of the emulsion of the lipids in the blood may be made. It is well known that a high level of blood lipids does not result in visible changes in the fundus in most cases. While the permeability of the arteries and the veins may be one factor, component parts of the emulsion are probably another. Further investigation may be necessary in order to determine other reasons for emulsification of the lipids of the blood in lipemia. Lipemia retinalis is simply the visual manifestation of an emulsion of blood fats.

## REPORT OF A CASE

A 6 year old white boy was admitted to Children's Hospital, Nov 16, 1936, because of abdominal cramps. There was no history of visual disturbance, ocular pain or inflammation. Routine examination revealed an enlarged spleen and liver and a mild fecal impaction, which was later relieved by a cleansing enema. Samples of blood taken for Wassermann and agglutination tests had the appearance of a creamy emulsion. Wassermann, Kahn and Mantoux reactions were negative. Roentgenograms of the abdomen showed a slightly enlarged liver and a considerably enlarged spleen. The result of a galactose tolerance test of hepatic function

### Dextrose Tolerance Test, Mg per 100 Cc

Fasting	91
½ hour	250
1 hour	175
2 hours	103
3 hours	90

was normal. Roentgenograms of the long bones showed no changes. Repeated examinations of the urine failed to reveal sugar, acetone, diacetic acid and albumin. The blood cell count was normal, and the basal metabolic rate was within normal limits.

Vision in both eyes was 6/6. Examination of the fundi showed severe lipemia retinalis in each eye. With a slit lamp the anterior segment of each eye appeared

<sup>10</sup> Bernstein, S. S., Williams, H. H., Hummel, F. C., Shepherd, M. L., and Erickson, B. H. *J. Pediat.* **14**, 570, 1939.

Candidate's thesis for the American Ophthalmological Society, 1943.

<sup>1</sup> Heyl, A. G. *Philadelphia M. Times* **10** 318, 1880, *Tr. Am. Ophth. Soc.* **3** 54, 1880.

<sup>2</sup> Wagener, H. P. *Am. J. Ophth.* **5** 521, 1922.

<sup>3</sup> Chase, L. A. *Diabetic Lipaemia Retinalis. Report of Case*, *J. A. M. A.* **97** 171 (July 18) 1931.

<sup>4</sup> Kollner, K. *Centralbl. f. prakt. Augenh.* **34** 212, 1910, *Ztschr. f. Augenh.* **27** 411, 1912.

<sup>5</sup> Parker, W. R., and Culler, A. C. *Am. J. Ophth.* **13** 573, 1930.

<sup>6</sup> McKee, S. H., and Rabinowitch, I. M. *Canad. M. A. J.* **15** 530, 1931.

<sup>7</sup> Lepard, C. W. *Am. J. Ophth.* **16** 12, 1933.

<sup>8</sup> Hardy, W. F. *Tr. Am. Ophth. Soc.* **19** 229, 1921, *Am. J. Ophth.* **7** 39, 1924.

<sup>9</sup> Marble, A., and Smith, R. M. *Blood Lipids in Lipaemia Retinalis*, *Arch. Ophth.* **15** 86 (Jan) 1936.

normal The blood stream of the smaller vessels of the conjunctiva had the appearance of a creamy emulsion, which made the identification of blood cells difficult

The patient was placed on a measured low fat diet consisting of 45 Gm of protein, 18 Gm of fat and 210 Gm of carbohydrate The high fat diet consisted of 45 Gm of protein, 100 Gm of fat and 30 Gm of carbohydrate Results are shown in table 1

TABLE 1—Analyses of the Blood Lipids in a Case of Essential Hyperlipemia\*

	Low Fat Diet	High Fat Diet
Plasma (mg per 100 Cc )		
Total lipid	3,159	9,370
Phospholipid	436	838
Neutral fat	2,166	7,636
Free cholesterol	129	199
Cholesterol esters	428	702
Erythrocytes (mg per 100 Gm )		
Total lipid	647	930
Phospholipid	481	583
Neutral fat	51	447
Free cholesterol	95	80
Cholesterol esters	20	15

\* From the Children's Hospital, Children's Fund of Michigan Research Division

He was maintained on a low fat diet, under which the spleen and the liver gradually decreased in size This boy continued in school with normal activities and on Feb 12, 1943 returned to the hospital, at which time a sample of blood was taken The results of these examinations closely parallel those of the original studies, as seen in table 2

TABLE 2—Low Fat Diet Consumed at Home

Plasma (mg per 100 Cc )	
Phospholipid	487
Free cholesterol	162
Cholesterol esters	351
Erythrocytes (mg per 100 Gm )	
Phospholipid	388
Free cholesterol	89
Cholesterol esters	95

Lipemia retinalis was present during the entire time the patient was under observation On a low fat diet it could be recognized only in the smaller divisions of the central artery and vein in the more peripheral portions of the fundus of each eye With a high fat diet the arteries and the veins throughout their entire extent were increased to twice their size and approached a common creamy color, so as to be indistinguishable from each other

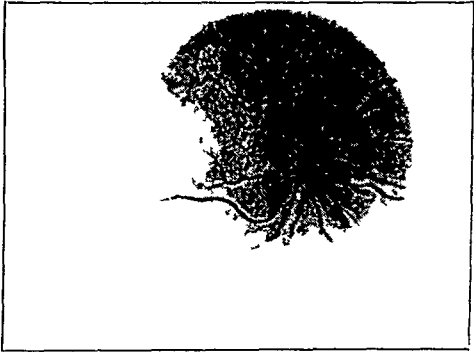
TABLE 3—Percentage of Total Fat

	Low Fat Diet		High Fat Diet
Plasma			
Neutral fat	68	increased	81
Phospholipid	14	decreased	9
Free cholesterol	4	decreased	2
Cholesterol esters	14	decreased	7
Erythrocytes			
Neutral fat	8	increased	48
Phospholipid	74	decreased	41
Free cholesterol	14	decreased	9
Cholesterol esters	3	decreased	2

From table 1 it is seen that there was a more striking increase in the total lipid content of the plasma than of the erythrocytes The percentage of neutral fat in both the plasma and the erythrocytes (table 3) showed a distinct in-

crease when the patient was on the high fat diet, while at the same time the percentages of cholesterol esters, phospholipid and free cholesterol were slightly decreased The percentage of neutral fat of the erythrocytes was increased far more than that of the plasma when fat was added to the diet When the emulsion contained a relatively high percentage of neutral fat, the lipemia retinalis was severe When the state of the emulsion changed under a low fat diet containing a relatively small percentage of neutral fat, the ophthalmoscopic examination showed only a slight degree of lipemia retinalis

The patient had acidosis for a small part of the time while under observation Acidosis may have resulted from abnormal fat metabolism, however, in this and in my previous case<sup>1</sup>



A photograph showing the appearance of the fundus of the patient on a high fat diet Note the increase in size of the blood vessels and how they stand out in relief beyond the disk This photograph was supplied by Dr F L Ryerson

It had no relation to the occurrence or the degree of lipemia retinalis Acidosis seems to be of secondary interest

Lipemia retinalis has been observed in a non-diabetic person with lipemia, whose renal and hepatic functions were normal (Holt, Aylward and Timbus<sup>11</sup>) For this patient also neutral fat levels were high The authors stated the belief that neutral fat was not normally disposed of and was accumulated in the phagocytic cells of the reticuloendothelial system, which resulted in an enlargement of the liver and the spleen

SUMMARY

Although lipemia retinalis is usually seen in the young person with severe diabetes, it is a phenomenon resulting from a rise in the level of the blood lipids and may occur in the presence of normal carbohydrate metabolism

Blood lipids composed of a high percentage of neutral fat seem more likely to produce characteristic retinal changes than do those composed of a low percentage of neutral fat

11 Holt, L E , Aylward, F X, and Timbus, H G J Clin Investigation 15 451, 1936



# JUVENILE AMAUROTIC FAMILIAL IDIOCY

## ITS OCULAR PATHOLOGY

ISADORE GIVNER, M.D., AND LEON ROIZIN, M.D.  
NEW YORK

Cerebromacular degeneration, or the juvenile form of amaurotic familial idiocy, was first described by Batten<sup>1</sup> in 1903. The clinical features of this disease were progressive loss of the intellectual faculties, loss of vision and loss of motor power. This condition differed from Tay-Sachs disease (infantile amaurotic familial idiocy) by the fact that cases did not occur predominantly in the Jewish race, that blindness was not associated with the same typical picture of the fundus, that its first clinical manifestations appeared at a later age and that the progress was slower. In 1905 Vogt<sup>2</sup> described the morbid anatomy, and Spielmeyer,<sup>3</sup> in the same year, reported cases of a condition resembling retinitis pigmentosa in which the pigmentary changes were thought at first to be a complication of the disease.

In 1908 Stock<sup>4</sup> first published the histologic changes in the eye in 3 of Spielmeyer's original cases. He noted that the optic nerves were normal and expressed the belief that this is a characteristic which distinguishes it from Tay-Sachs disease and retinitis pigmentosa. The only case in this country in which the histologic changes in

the eye were described is that reported by Wandless,<sup>5</sup> but no photographs were included.

Through permission of Dr. Rayford K. Adams, an unusual opportunity was had to observe 2 patients, a brother and a sister, with this condition. The girl died Sept. 15, 1942, and on her death the globes and brain were secured for study. At about this time a second patient died of the disease, and material was likewise made available for histologic study.

Since we studied the fundi and made photographs only of the girl, the usual histopathologic studies made in this case are reported in case 1. Material in the second case was kept for investigation of the histochemical nature of the lipids.

### REPORT OF CASES

**CASE 1**—D. N., a girl, was admitted to the New Jersey State Village for Epileptics on Aug. 29, 1940. She was the sixth of 7 children. The younger brother of the patient also has cerebromacular degeneration and is still a patient in the Village. Her history, taken from the records of the institution, is as follows: "The patient was born May 31, 1923. She was normal until the age of 4 years, when she began to have trouble with vision. She was thought to be mentally deficient at that time. She had 'spasms' shortly after birth but had no more convulsions until the age of 13 years. Her eyesight faded entirely. She attended school for the blind for one and a half years and learned to read Braille."

**Ophthalmoscopic Examination**—The lens of the right eye had fine gray opacities at the posterior pole, the lens of the left eye was normal. Convergent strabismus with rotary nystagmus was present in the left eye. Both fundi showed optic nerve atrophy. The vessels were very thin. The maculas had areas of depigmentation and condensation. Scattered over the fundi of both eyes were clumps of pigment. Some resembled bone corpuscles in shape, others were less well defined (fig. 1). Vision was limited to light perception. The patient died Sept. 15, 1942, at the age of 19 years.

**Histopathologic Study of Eyes**—The globes were fixed in a 10 per cent concentration of dilute solution of formaldehyde for forty-eight hours and then in Zenker's solution. They then were dehydrated in the usual way and fixed in both pyroxylin and paraffin. The entire retina was involved, but to different degrees. No uniformity in the intensity of involvement was noted.

5 Wandless, H. W. Amaurotic Family Idiocy. A Preliminary Report of Three Cases, New York M. J. 84: 953, 1909.

Read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, Nov. 15, 1943.

From the Department of Neuropathology of the New York State Psychiatric Institute and Hospital.

1 Batten, F. E. Cerebral Degeneration with Symmetrical Changes in the Maculae in Two Members of a Family, Tr. Ophth. Soc. U. Kingdom 23: 386, 1902-1903.

2 Vogt, H. Ueber familiäre amaurotische Idiotie und verwandte Krankheitsbilder, Monatschr. f. Psychiat. u. Neurol. 18: 161 and 310, 1905.

3 Spielmeyer, W. Ueber familiäre amaurotische Idioten, Neurol. Centralbl. 24: 620, 1905; Weitere Mittheilung über eine besondere Form von familiärer amaurotischer Idiotie, ibid. 24: 1131, 1905; Ueber familiäre amaurotische Idioten, Arch. f. Psychiat. 40: 1038, 1905; Klinische und anatomische Untersuchungen über eine besondere Form von familiärer amaurotischer Idiotie, in Nissl, F., and Alzheimer, A. Histologie und Histopathologie, Jena, G. Fischer, 1908, vol. 2, p. 193.

4 Stock, W. Ueber eine bis jetzt noch nicht beschriebene Form der familiär auftretenden Netzhautdegeneration bei gleichzeitiger Verblödung und über typische Pigmentdegeneration der Netzhaut, Klin. Monatsbl. f. Augenheilk. 46: 225, 1908.



Here and there small portions were less severely damaged than the retina around them.

The most prominent change was the diminution in width of the internuclear layer, in some portions the inner and the outer nuclear layer were juxtaposed (fig 2). The choroid appeared normal (fig 3). The pigment epithelium showed many changes. An irregular loss of pigment within the cells was associated with

and cones seemed to lie in an organized mass of detritus, the individual elements being practically nonexistent, except here and there. The pigment and nuclei, like those of the pigment epithelium, were scattered through this mass of tissue. This change did not occur post mortem, as the globes were fixed soon after death (fig 4). In many places the outer limiting membrane could not be recognized. The outer

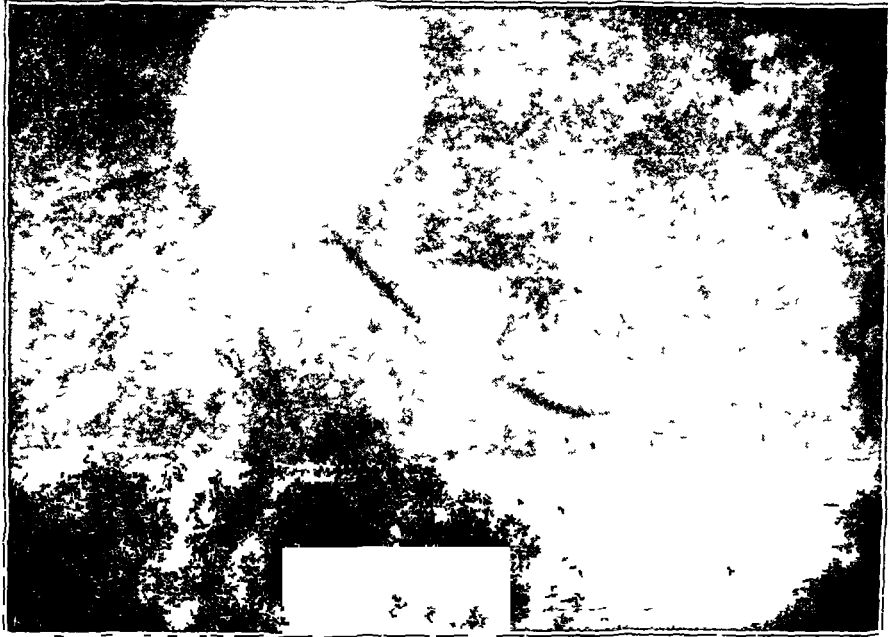


Fig 1—Photograph of the fundus in case 1, showing optic nerve atrophy, narrowed vessels and clumping of pigment.



Fig 2—Juxtaposition of the inner and the outer nuclear layers, with no remaining internuclear layer.

scattering of its granules at the site of the rods and cones in large, dense spherical masses. The pigment cells at the same time became flattened, less regularly arranged and in some places heaped into two or more layers. The nuclei of the pigment epithelium were fairly normal in appearance but in places seemed shrunken and irregular and stained deeply. The most striking change was in the depigmentation. The rods

nuclear layer was notably affected, as evidenced by irregularity of arrangement, smaller, shrunken cells, and sparseness. The inner nuclear layer was less affected but was also involved, and, as was said before, the internuclear layer was frequently absent (fig 5). The ganglion cell layer showed no diminution in number of cells, but structural changes were observed. Some ganglion cells were swollen and others spherical, some

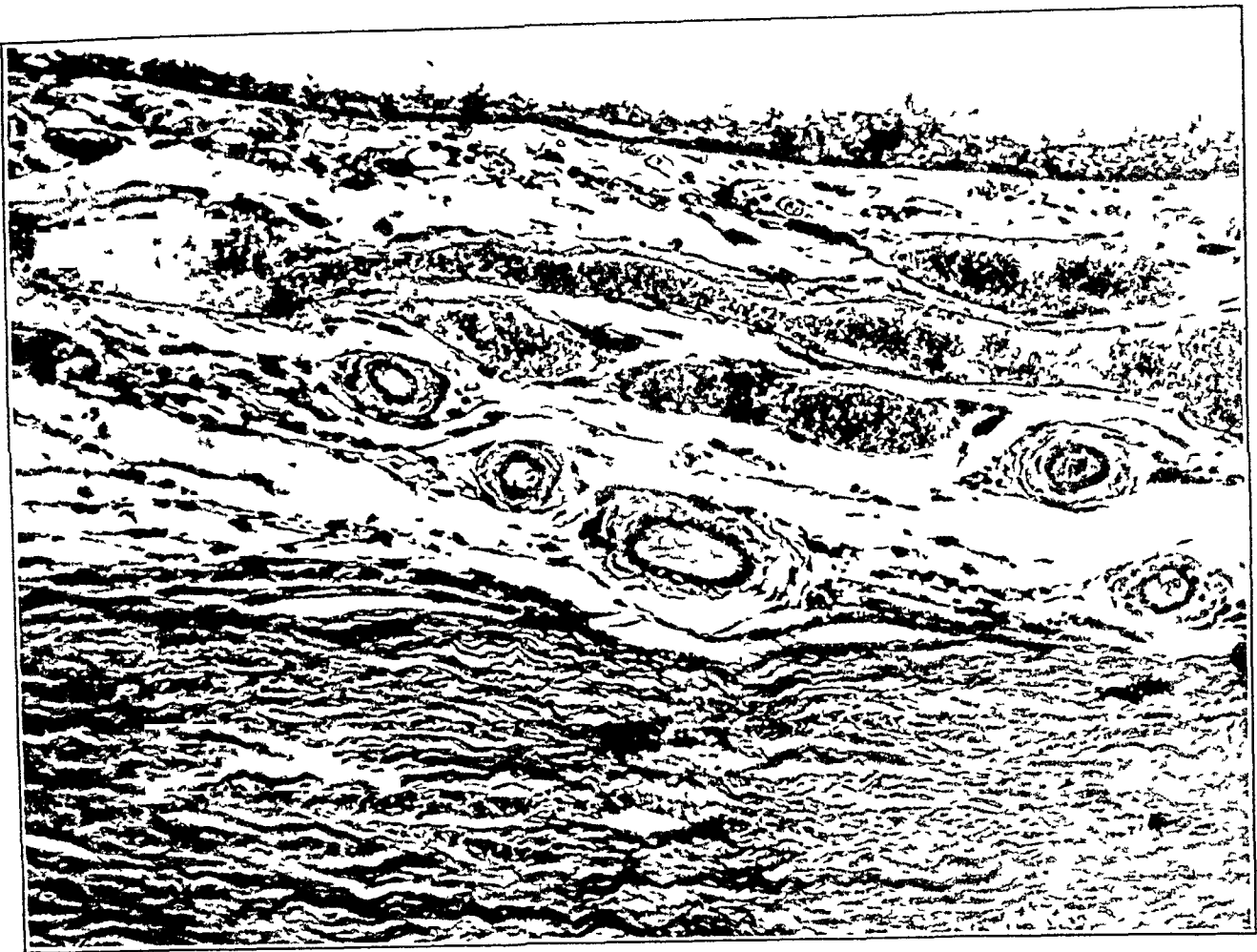


Fig 3—Normal choroid

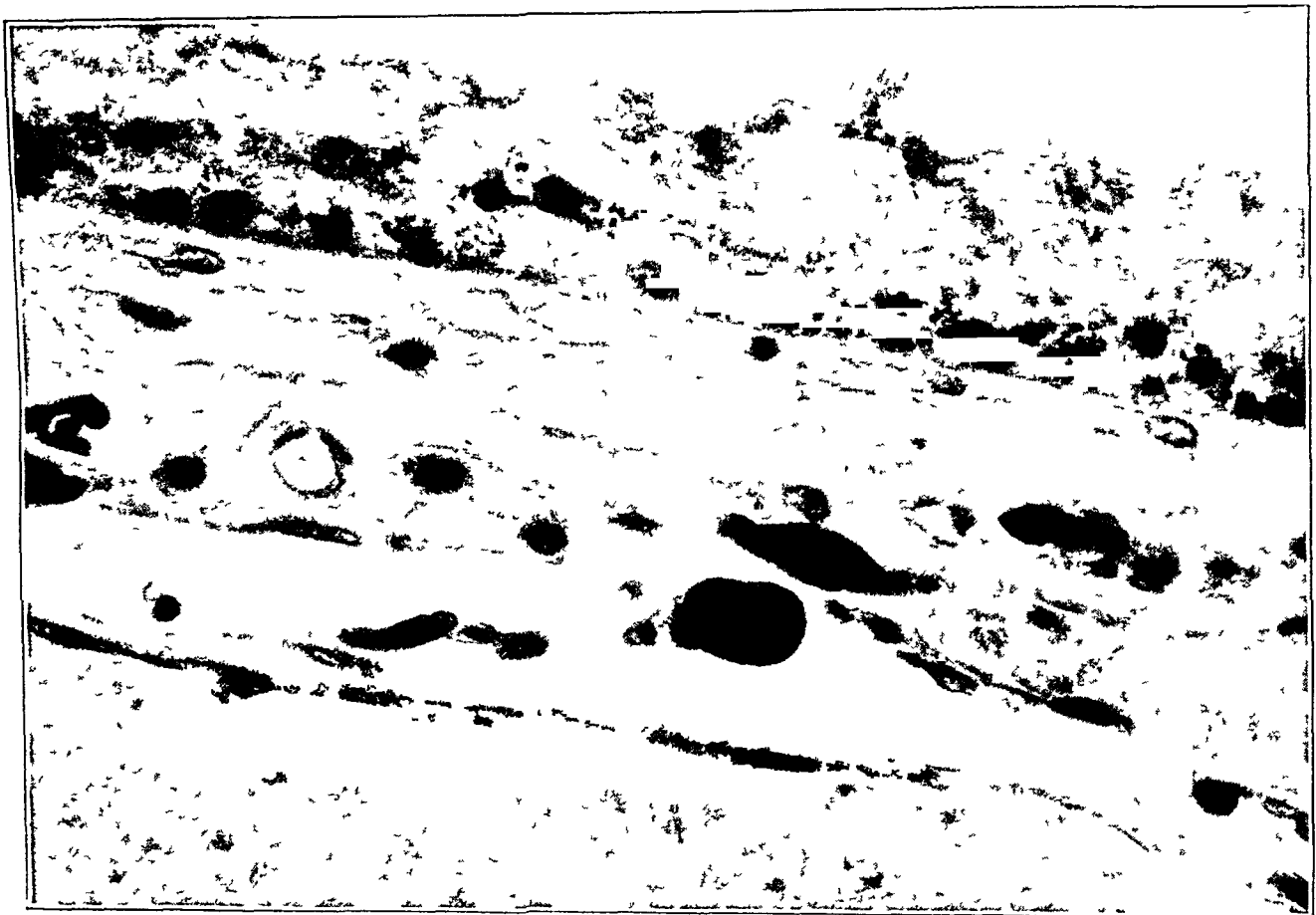


Fig 4—Scattering of pigment of the pigment epithelium and replacement of the layer of rods and cones by an organized mass of detritus

contained granular masses, others, eccentric nuclei, and in some, vacuoles, as described in cases of Mayou and Ichikawa, were noted (fig 6) The nerve fiber layer showed an increase of glial tissue, as did most of the retina proper, where the neuroglia replaced degenerated layers The retinal vessels showed questionable splitting

atrophy was absent in Spielmeyer's cases Brooks, in the case published by Wandless, observed no ganglion cells in the retina or nerve fibers in the optic nerves, but Marchi's method revealed droplets of fat in the optic nerve,

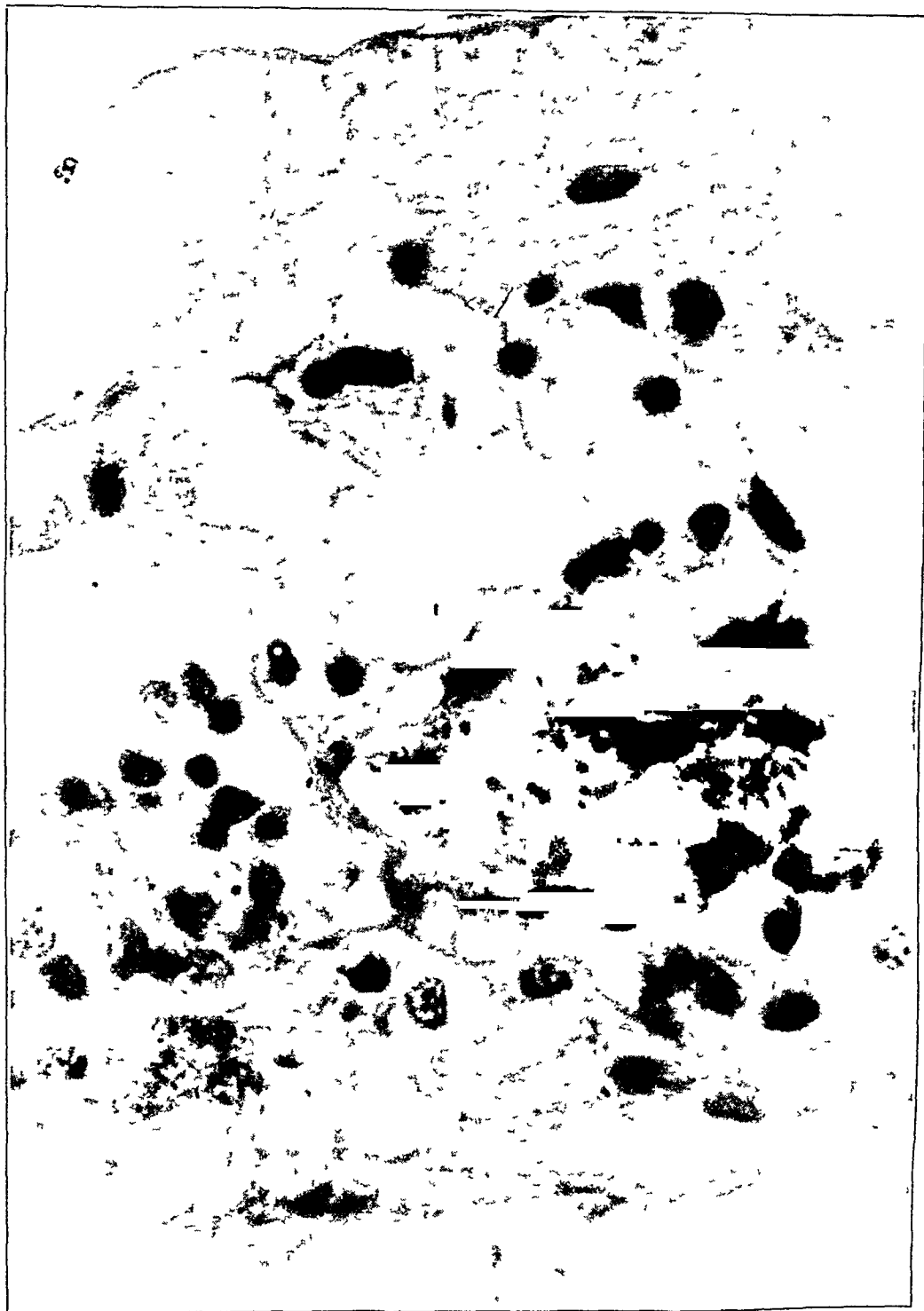


Fig 5—Typical section of the retina, showing disorganization with resulting loss of the internuclear layer and clumping of pigment

of the elastic fibers Stock noted slight endarteritis in Spielmeyer's cases

The optic nerve showed definite areas of atrophy, as shown by the Smith-Quigley stain (fig 7)

Torrance described 3 cases, in all of which optic nerve atrophy was present Optic nerve

which he concluded indicated degenerated fibers Examination of a ganglion cell accompanying a ciliary nerve showed no pathologic changes

Various observers have attempted to determine which change was primary and which secondary and have tried to draw conclusions

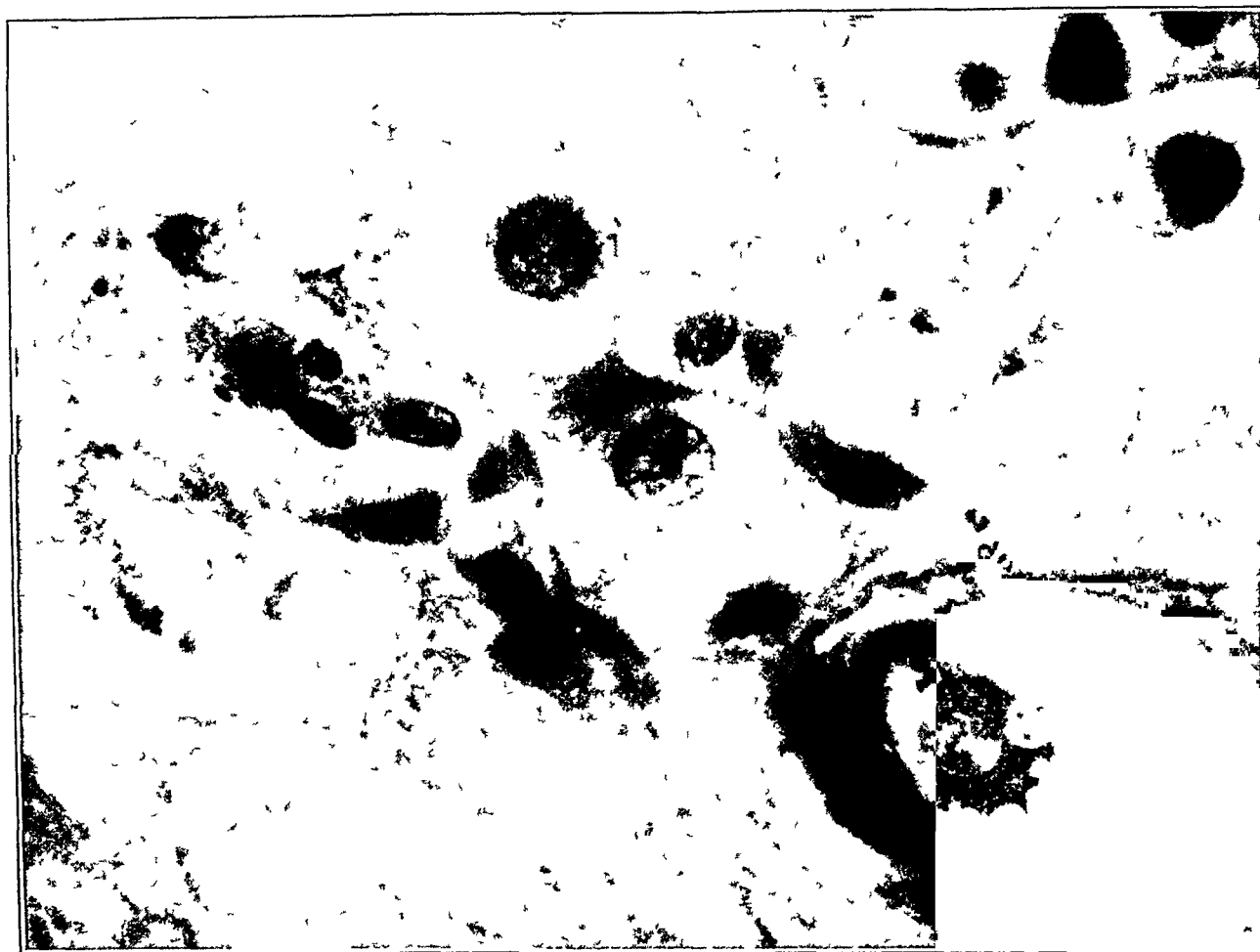


Fig 6—Ganglion cells of the retina, one of which shows two large vacuoles in the cytoplasm



Fig 7—Optic nerve atrophy, as demonstrated by the Smith-Quigley stain

from their own cases Stock concluded that the changes were due to primary degeneration of the neuroepithelium and secondary proliferation, combined with regressive changes in the pigment epithelium Ichikawa<sup>6</sup> interpreted the changes as a uniform degeneration of all the

and Paton<sup>7</sup> expressed the belief that the earliest lesion was a breaking up of the rods and cones, associated with rarefaction and narrowing of the outer nuclear layer, the cell bodies to the outer nuclear layer being affected first and the afferent and efferent processes next The degenerated

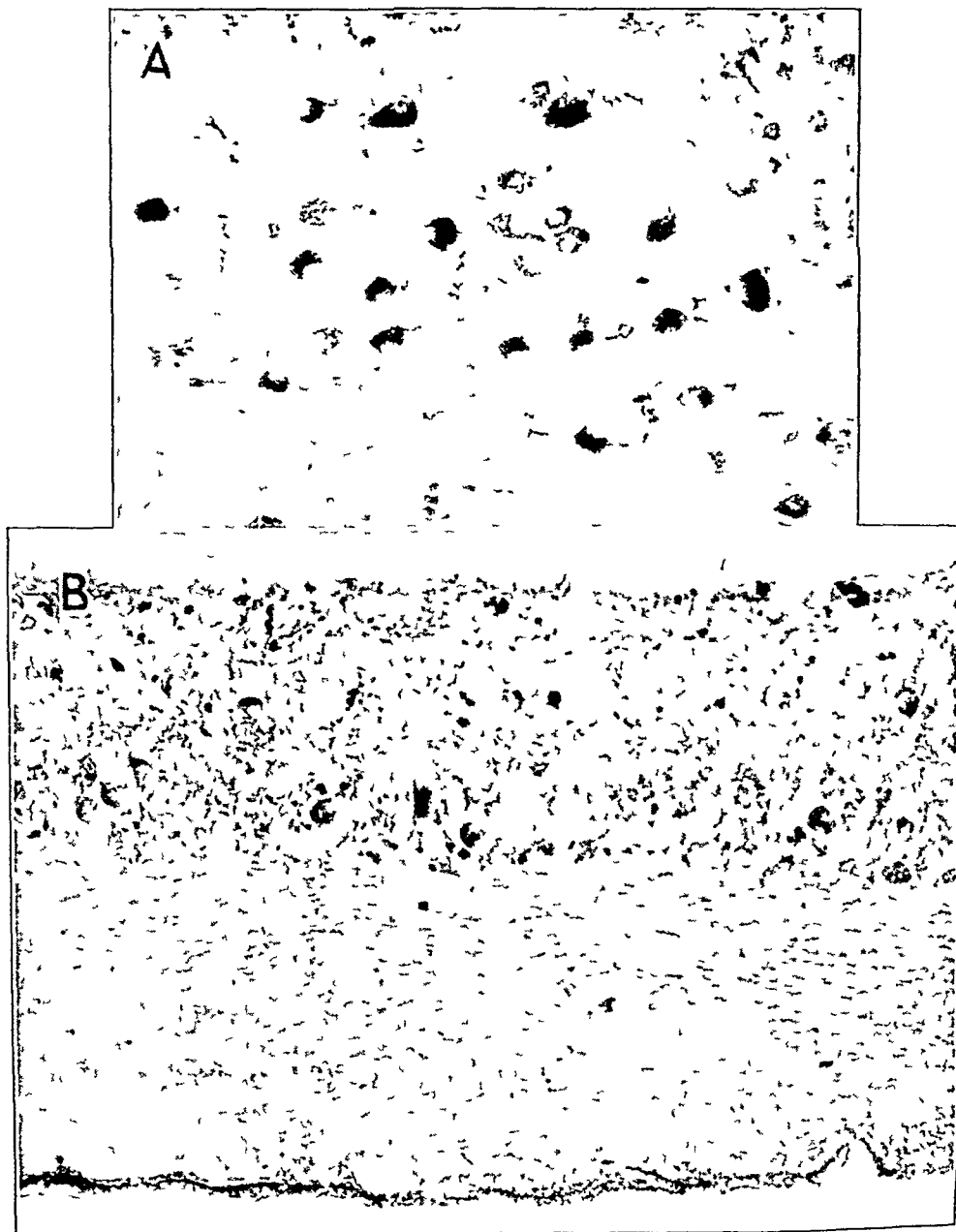


Fig 8—Intracellular fatty products (A) in the ganglion cells of the cerebral cortex and (B) in the ganglion cells of the retina Sudan black B, low power magnification

nervous elements of the retina—similar to that which occurs with retinitis pigmentosa Holmes

6 Ichikawa, K Ueber eine der amaurotischen familiären Idiotie verwandte Krankheit mit histologischer Beschreibung, nebst einem Beitrag zur Kenntnis der Beziehung zwischen erblichen Augenkrankheiten und zur Pathogenese der primären Cyste der Pars ciliaris, *Klin Monatsbl f Augenh* 47 73, 1909

external layers of the retina were replaced by proliferating neuroglia, followed by overgrowth of the pigment epithelium, with invasion of the degenerating retinal layers The changes in the pigment cell layer were said to be secondary to the lesion in the other layers of the retina

7 Holmes, G, and Paton, L Cerebro-Macular Degeneration (the Juvenile Form of Amaurotic Family Idiocy), *Tr Ophth Soc U Kingdom* 45 447, 1925

Mayou,<sup>8</sup> who examined the eye in 1 of Batten's cases, in which there was complete disappearance of the ganglion cells, expressed the belief that the disease commenced here, where the cells swelled, lost their Nissl substance, became vacuolated and eventually disappeared. This was followed by edema of the internuclear layer, by

mentation. Greenfield and Holmes<sup>9</sup> best summarized the seeming discrepancy by concluding that all the cases reported can be placed in one of three groups

(1) Cases similar to those of Stock, Bielschowsky and Holmes, in which only the outer layers of the retina suffer and changes in the

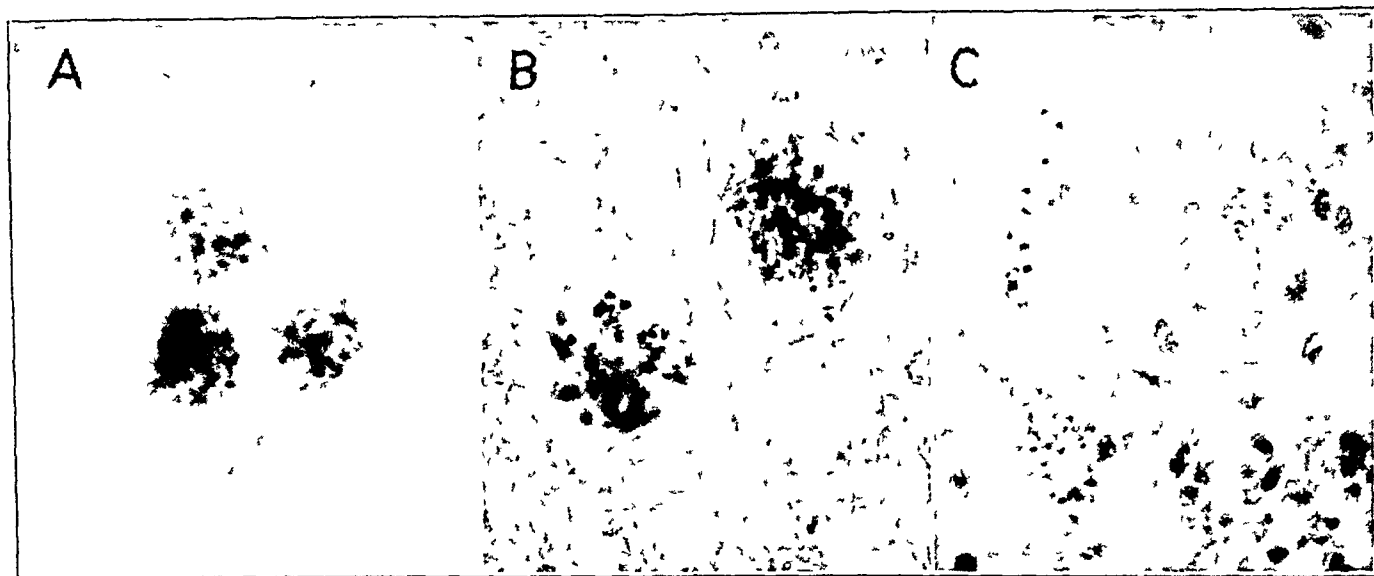


Fig 9—Prelipid products (A) in the ganglion cells of the cerebral cortex, (B) in the Purkinje cells of the cerebellum (modified Schaffer method) and (C) safranophilic granules in a Purkinje cell and its apical dendrite (safranin stain). High power magnification.

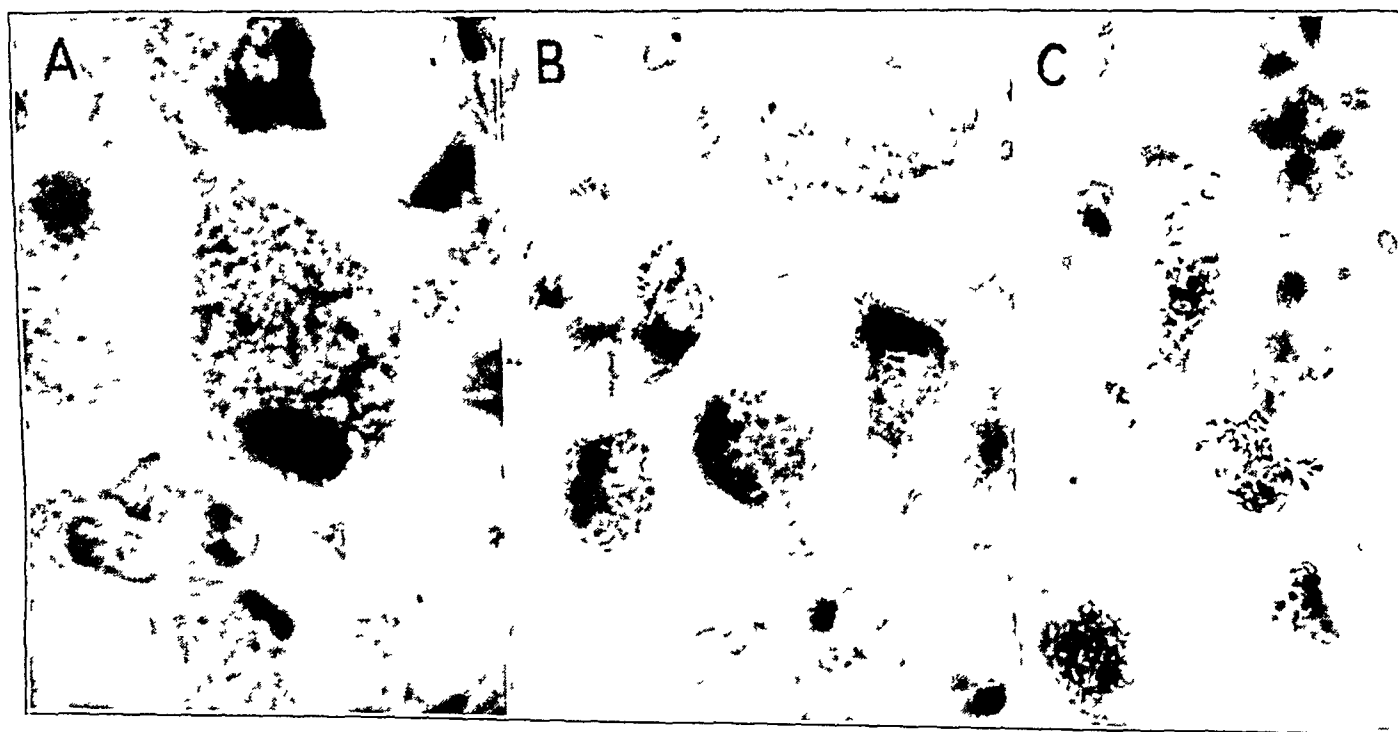


Fig 10—Ganglion cells of the retina (A) argentophilic products (modified Bielschowsky method), (B) prelipid products (modified Schaffer method) and (C) safranophilic granules mixed with some pigment (safranin stain). High power magnification.

gradual disappearance of the outer nuclear layer and of the rods and cones and, finally, by pig-

mentation. inner layers are probably secondary, (2) cases of Mayou, Didé and Torrance, with changes in the inner layers, especially the ganglion cells, sometimes associated with changes in the rods and cones, and (3) cases of Brooks and Ichi-

<sup>8</sup> Mayou, M. S. Cerebral Degeneration, with Symmetrical Changes in the Maculae, in Three Members of a Family, *Tr Ophth Soc U Kingdom* 24 142, 1905. Batten, F. E., and Mayou, M. S. Family Cerebral Degeneration with Macular Changes, *Proc Roy Soc Med (Ophth Sect)* 8 70, 1914-1915.

<sup>9</sup> Greenfield, J. G., and Holmes, G. The Histology of Juvenile Amaurotic Idiocy, *Brain* 48 183, 1925.

kawa in which all layers are severely degenerated

Greenfield and Holmes concluded that the retinal changes may be defined as a primary change in the ganglion cells combined with independent degeneration of the outer neurotic elements of the retina, which in some cases extends to the inner nuclear and inner reticular layers. This degeneration is followed by glial sclerosis and proliferation of pigment epithelium cells, which wander into the degenerated tissue.

The involvement of the outer layers distinguishes the retinal lesions of the juvenile from the infantile type of familial amaurotic idiocy.

**CASE 2**—The disease in this case was similar to the Batten-Mayou type of cerebromacular degeneration. The patient, a first child, was born on Sept 30, 1928. In 1935, at the age of 7, he began to have trouble with his eyes. The macular region of the right eye presented a picture of degeneration. Physical examination at this time revealed nothing abnormal. At the age of 8 years convulsions appeared.

He was admitted to the Village on April 8, 1942, at the age of 14 years. Convergent strabismus with nystagmus was noted. Vision was limited to light perception. He was disoriented for time, place and persons. He had frequent convulsions and died on Sept 20, 1942. Simultaneous comparative histopathologic and histochemical studies were made on the ganglion cells of the central nervous system and those of the retina. Microscopic examination was carried out with the usual technics, including the Nissl, the hematoxylin and eosin and the Bielschowsky modified method for nerve cells, the Cajal, Hortega and Holzer methods for the various types of glia cells, Spielmeyer's stain for myelin sheaths, and Bodian's stain for neurofibrils. In addition, numerous stains for fatlike substances (scarlet R, sudan III, sudan black B, osmic acid and the Lorrain-Smith and Smith-Dietrich technics) and for hematoxylinophilic and safranophilic bodies (iron hematoxylin and safranin) and stains of the aniline series for special granular products were applied. Some histochemical studies were also based on histochemical properties of the fat products for polarized light and their solubility in various fatty solvents.

The chief microscopic observations on the central nervous system being similar in the 2 cases, one description will suffice. Throughout the gray matter of the central nervous system typical nerve cell changes were seen—pronounced tigrolysis, complete disappearance of the Nissl bodies, displacement of the nucleus, pear-shaped and balloon-shaped neurons, satellitosis and neuronophagia. Silver impregnation methods disclosed various stages of fibrillary changes in the neurons and their processes. Involvement of nerve cells in the cortex and in the various gray centers of the brain varied in intensity and extent. The cerebellum disclosed slight degeneration of the elements of the granular layer, being more pronounced in the Purkinje cells.

The cytoplasmic network of altered cells was filled at times with a granular material, which was particularly well demonstrated in frozen sections stained by methods for fatlike substances, these granules stain orange or mar red with scarlet R and sudan III, at times slightly greenish with sudan black B, grayish with osmic acid and faintly bluish with Nile blue sulfate. Lipid granules were present, also, in the apical processes of the neurons

of the cortex, they were particularly conspicuous in the Purkinje cells, which showed the most advanced stages of degeneration.

The solubility of the fatlike products were tested with various solvents. This material failed to dissolve after several hours (two to six hours) of immersion in cold alcohol, ether and acetone respectively. After treatment with xylene and benzene for one-half to one hour, the granules stained much more faintly with scarlet R, sudan III and sudan black B. Hot alcohol, a mixture of chloroform and methanol, as well as pyridine, appeared to dissolve the granules completely. Sections stained with safranin<sup>10</sup> as well as with stains of the aniline series<sup>11</sup> and iron hematoxylin,<sup>12</sup> showed in some cells the presence of fine granular products (safranophilic or anilinophilic and prelipid granules). Figures 8, 9 and 10 illustrate the presence of intracellular fatlike material and granular products in the ganglion cells of the cortex and of the retina. The histochemical reactions, as evidenced by the aforementioned methods, seemed to point to the presence in both the brain and the retina of the same type of lipids, i. e., a mixture of phosphatides and cerebroside.

#### COMMENT

With respect to the histopathologic and clinical interrelations or the differentiation of the several types of amaurotic familial idiocy, we agree with Globus<sup>13</sup> that "while minute studies in certain cases may often disclose deviations from the typical pathology of clinical pictures, they nonetheless fail to establish sharp boundaries between a given case and other members of the entire group."

From an etiopathogenic point of view, Sachs's<sup>14</sup> concept that the disease is a disturbance of the nervous system of primary and degenerative character still stands true even if viewed in the light furnished by recent investigations. Schaffer's<sup>15</sup> hypothesis that it is a heredodegenerative disease restricted only to neuroectodermal derivatives and transmitted through the hyaloplasm does not seem in our opinion to be supported by our observations, in view of the involvement of elements of mesodermal nature—the microglia and the reticulo-endothelial system—which has been reported by

10 Dide, M., and van Bogaert, L. Sur l'idiotie amaurotic juvenile (type Spielmeyer-Vogt), *Rev. neurol.* **69** 1, 1938.

11 Jervis, G. A., Roizin, L., and English, W. H. Juvenile Amaurotic Idiocy, *Psychiatric Quart.* **16** 132, 1942.

12 Schaffer, K. Tatsachliches und Hypothesisches aus der Histopathologie der infantile-amaurotischen Idiotie, *Arch. f. Psychiat.* **54** 570, 1921-1922.

13 Globus, J. H. Amaurotic Family Idiocy, *J. Mt. Sinai Hosp.* **9** 451, 1942.

14 Sachs, B. On Amaurotic Family Idiocy. A Disease Chiefly of the Gray Matter of the Central Nervous System, *J. Nerv. & Ment. Dis.* **30** 1, 1903.

15 Schaffer, C. General Significance of the Tay-Sachs Disease, *Arch. Neurol. & Psychiat.* **14** 731 (Dec.) 1925.

other investigators (Pick and Bielschowsky<sup>16</sup>, Bielschowsky<sup>17</sup>, Jervis, Roizin and English,<sup>11</sup> and others) This hypothesis, however, remains open for further study (Sachs<sup>18</sup>, Hassin<sup>19</sup>, Globus,<sup>20</sup> and others) Gordon's,<sup>21</sup> and particu-

larly Marburg's,<sup>22</sup> assumption that an endogenous factor, of hormonal origin (adrenal, medullary portion, and thymus), is involved and that the "lack of respective esterases is the probable cause of the damage of the nervous system" needs confirmation

In conclusion, the histochemical reactions as evidenced by our investigation, in both the retina and the brain, point to the presence in the involved cells of the same type of lipids, i.e., a mixture of phosphatides and cerebroside

16 Pick, L., and Bielschowsky, M. Ueber die lipoidzellige Splenomegalie (Typus Niemann-Pick) und amaurotische Idiotie, *Klin Wchnschr* 6 1631, 1927

17 Bielschowsky, M. Amaurotische Idiotie und lipoidzellige Splenohepatomegalie, *J f Psychol u Neurol* 36 103, 1928

18 Sachs, B. Amaurotic Family Idiocy and General Lipoid Degeneration, *Arch Neurol & Psychiat* 21 247 (Feb) 1929

19 Hassin, G. B. Amaurotic Family Idiocy (Infantile Type of Tay-Sachs), in *Histopathology of the Peripheral and Central Nervous Systems*, ed 2, New York, Paul B Hoeber, Inc., 1940, p 353, *Histopathologic Observations on the Changes of the Eyes in a Case of Amaurotic Family Idiocy (Infantile Type of Tay-Sachs)*, *J Mt Sinai Hosp* 9 536, 1942, *Niemann-Pick Disease Pathologic Study of a Case*, *Arch Neurol & Psychiat* 24 61 (July) 1930

20 Globus, J. H. Amaurotic Family Idiocy, in Penfield, W. *Cystology and Cellular Pathology of*

108 East Sixty-Sixth Street

722 West One Hundred and Sixty-Eighth Street

the Nervous System, New York, Paul B Hoeber, Inc., 1932, vol 3, p 1166, footnote 13

21 Gordon, A. Cases Allied to Amaurotic Family Idiocy, with Remarks on the Genesis of the Affection, *New York M J* 85 294, 1907

22 Marburg, O. Studies on the Pathology and Pathogenesis of Amaurotic Family Idiocy, *Am J Ment Deficiency* 46 312, 1942



# INTRACAPSULAR EXTRACTION OF SENILE CATARACT

MATHRA DAS PAHWA, MD

LAHORE, INDIA

I have performed 170,000 operations for cataract, almost all of them intracapsular extractions, and the method which I have followed throughout was devised by me shortly after I began ophthalmic surgery

The controversy as to the use of the intracapsular or the extracapsular operation is always going on in all countries, Indian surgeons as a whole, especially the ophthalmic surgeons in the Punjab, have always favored the intracapsular method, while in some localities the extracapsular operation is the rule, although some surgeons in Europe have adopted the intracapsular operation as a routine in their clinics

The advantages of the intracapsular method may be presented as follows (1) It does not require two operations, (2) the operation can be performed even when the cataract is not completely mature, (3) as there are no shreds of capsule or lens matter to be caught in the edges of the wound, the chances of subsequent iritis and cyclitis are reduced to the minimum, and (4) ultimate vision after an intracapsular operation is much better than after extracapsular extraction

There is one disadvantage, loss of vitreous, which, if it does occur, is not a serious matter. It is this accident, however, which has led many surgeons to abandon the operation

I have perfected intracapsular delivery of the lens by the tumbling method, and all the ophthalmic surgeons who have visited my clinic are impressed with the rarity of the loss of vitreous

## OPERATION

This operation is the method of choice with me and many surgeons have been trained in my clinic because of its remarkable simplicity, its freedom from complications and little instrumentation. It is suitable for all types of senile cataract, whether mature or not, hard or morgagnian

As this operation is simple, it requires few instruments. These consist of speculum, a pair of fixation forceps, cataract knife, iris forceps, a pair of iris scissors, two squint hooks, iris spatula, scoop and cystotome. The last three instruments are kept simply as a precautionary measure

An assistant who knows what is expected of him at each stage is necessary

Read before the Indian Medical Association, Srinagar, Kashmir, India

*Anesthesia*—A 2 per cent solution of butacaine sulfate, 1 drop at a time, is instilled three or four times at three minute intervals before the operation. It gives a fairly complete anesthesia. I do not use facial block

*Section*—The patient is requested to lie down on the table. After insertion of the speculum, the eyelashes of the upper lid are cut with a pair of scissors, and the eye is irrigated with a 1/5,000 solution of mercury bichloride. The eye is fixed with fixation forceps. The knife is inserted at 9 o'clock (right eye) in the cornea at the side of the limbus, and is carried straight across the anterior chamber and brought out exactly at 3 o'clock. With the left eye, the section is from 3 to 9 o'clock. With gentle sawing movements, the knife is carried straight upward, and the section is finished about 1 mm below the upper border of the cornea

It will be obvious from this description that I believe in a low section, the scar is hidden by the lid and therefore is not a disadvantage. Also if a low section is made the delivery of the lens is much easier

With beginners, it is a common fault to press the eyeball with the fixation forceps, this should always be guarded against, and just before the section is finished the fixation forceps should be removed

*Iridectomy*—I perform iridectomy in all cases, this, again, makes the delivery of the lens easier. The iris is pulled out through the corneal wound with the iris forceps and cut with iris scissors

*Delivery of Lens*—At this stage the speculum is removed, and the assistant lifts the upper eyelid with a strabismus hook held in his right hand and pulls the lower lid down with the fingers of his left hand. The surgeon places his left thumb just above the eyebrow and slightly pulls it up, and in the other hand he holds the other strabismus hook. This hook is now applied to the sclera 2 mm below the junction, at about 6 o'clock. It is slowly drawn up toward the limbus with very slight backward pressure, which movement dislocates the lens. It is a mistake to apply too much pressure, a gentle touch is enough. If with the first attempt the lens is not dislocated, the pressure should be repeated. As soon as the lens is dislocated, the lower border of the lens will be seen in the anterior chamber. With the hook the lower pole of the lens is lifted up still farther until it presents in the corneal section

It will be gathered from the foregoing description that the lens turns a complete somersault before it is delivered, that is, the lower pole of the lens comes out first through the corneal wound, this constitutes "tumbling of the lens." I was the first to attempt extraction of the ordinary hard senile cataract by this technic. I have trained many operators from all parts of the world who follow this method, and I have

no doubt that the operation will gain still more in popularity

After the lens is delivered, the iris is carefully freed from the edges of the corneal wound and replaced either with the strabismus hook or with an iris spatula. The upper lid is lowered gently, the patient is warned in advance not to close his eyes tightly or in any way squeeze his eye. The eye is covered with a piece of cotton wool, and both eyes are bandaged.

*After-Treatment*—The patient should lie straight on his back and remain quite still for the first four to six hours, after which he is permitted to turn toward the normal eye. Unless there are indications which demand examination of the eye earlier, I generally inspect the eye on the seventh day, when the wound is healed, and the fellow eye is left uncovered.

On the tenth day, in the absence of complications, such as prolapse of the iris, ununited corneal wound or sepsis, the bandage is removed from the eye which has been operated on and the eye covered with a green shade.

#### SUMMARY

Like any other surgical procedure, a little patience and considerable practice are required before the art of neat delivery of the lens is mastered. Perseverance is essential, but if the technic is once mastered, the surgeon will have a simple, efficient and safe method of doing his cataract operations.

5 Temple Road

# INTRAOCULAR PRESSURE AND ITS RELATION TO RETINAL EXTRAVASATION

JOSEPH IGRERSHEIMER, MD

BOSTON

## HIGH AND LOW INTRAOCULAR PRESSURE IN RELATION TO RETINOPATHY

During my studies on anatomic changes of the optic nerve associated with general hypertension, I examined the eyes of a patient aged 42 who was admitted to a well known hospital four times in one and one-half years because of chronic glomerulonephritis with increased blood pressure and uremic attacks. On each new admission the nonprotein nitrogen of the blood was at a higher level, the last time being as high as 507 mg of urea and 91 mg of uric acid per hundred cubic centimeters. In spite of this enormous elevation of nonprotein nitrogen and the high blood pressure, ophthalmoscopic examination revealed no spots or hemorrhages in the retina, even later, examination of many anatomic slides showed only one tiny group of "ganglioform nerve fibers." On the other hand, one could follow the development of a glaucomatous (from a physiologic) cupping during life, and after the patient died this was demonstrated histologically. Elschnig, one of the greatest authorities on the pathologic anatomy of glaucoma, to whom I sent the slides, confirmed the observation of glaucomatous cupping in both eyes. Although, to my regret, tonometric measurements were lacking in the record, it is probable that the intraocular tension, too, was high. Thus, there was the combination of high blood pressure, an unusually large amount of nonprotein nitrogen in the blood, primary glaucoma and absence of retinopathy. The problem arises: Had the glaucoma anything to do with the absence of retinopathy? I am inclined to answer "yes." As far as I can learn, nothing is known about such a relation. By chance, however, I found 2 interesting observations in the literature. Grafe,<sup>1</sup> in 1924, described briefly a case of retinitis diabetica in one eye which gradually diminished with the

increase of intraocular tension in this eye, the other eye was glaucomatous for a long time, and in this eye diabetic retinitis never developed. Schieck,<sup>2</sup> in 1930, mentioned that retinitis albuminurica disappeared when glaucoma developed in the same eye. Both authors merely noted these observations but did not give them any serious consideration.

I personally saw a patient several months ago who probably belonged to this group. A Negro aged 79 had arteriosclerosis and general hypertension (blood pressure, 250 systolic and 160 diastolic). In September 1940 examination at the Massachusetts Eye and Ear Infirmary revealed pronounced, long-standing arteriosclerotic retinopathy with failing vision in both eyes and normal tension. I saw the patient for the first time on August 19, 1942, in the ophthalmic outpatient department of the Boston City Hospital. For six days she was totally blind in both eyes. She could not say whether she could see formerly with one or with both eyes. The right eye was very hard (tension, 65 mm [Schiotz]). The cornea was hazy. Only indirect ophthalmoscopic examination was possible, and this showed pronounced glaucomatous cupping but no retinal spots. The blind left eye had normal tension (14 mm [Schiotz]). The disk showed partial pallor, there were marked retinopathy and endovascular change. Several days later the tension in the right eye had been reduced almost to normal by miotics, the haziness of the cornea had disappeared, and I was able to see the fundus by direct ophthalmoscopic inspection. There were also many endarteritic vessels in this eye and numerous fine, yellowish spots in the retina, but, in contrast to the left eye, the latter were minute and in no way as striking as the brilliant whitish spots in the retina of the left eye. The difference in the appearance of the retina of the two eyes was notable in spite of the endovasculitis in both, and it is possible that the high tension in the right eye was responsible.

2 Schieck, F. Die Erkrankungen der Netzhaut, in Schieck, F., and Bruckner, A. Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1930, vol 5, p 425

Read at a meeting of the New York Society for Clinical Ophthalmology, April 5, 1943, and, in enlarged form, before the Section of Ophthalmology of the College of Physicians of Philadelphia, Jan 20, 1944.

1 Grafe, E. Die Bedeutung der Insulintherapie des Diabetes für die Ophthalmologie, Ber u d Ver-samml d deutsch ophth Gesellsch 44 53, 1924

I owe the following observation to Dr David Cogan, head of the Howe Laboratory of the Massachusetts Eye and Ear Infirmary

A man aged 82 was admitted on Sept 3, 1940, with the complaint of difficulty in reading, which had been worse in the past two or three weeks

**Right Eye** The pupil reacted sluggishly to light. The cornea was not steamy. Ophthalmoscopic examination revealed considerable arteriosclerosis, with obstruction of veins at the arteriovenous crossings and many flame-shaped hemorrhages. The optic cup was not glaucomatous. Vision was 20/100, and tension was 14 mm.

**Left Eye** The pupil of this eye was similar to that of the right eye. The cornea was steamy. There was marked glaucomatous cupping. No hemorrhages were seen. Vision was uncertain, and tension was 28—mm.

**October 16** The field of the right eye was constricted. Vision was 18/200 with the patient's own glass. Vision in the left eye was limited to ability to count fingers at 2 feet (60 cm). Only part of the temporal field remained. No hemorrhages were seen in this eye. The blood pressure was 160 systolic and 80 diastolic.

**November 5** Vision was unchanged. Ophthalmoscopic examination showed a condition similar to that in the previous examination. Tension was 15 mm in the right eye and 26 mm in the left eye.

In this case, too, a marked difference in tension in the two eyes was noted, in the right eye it was rather low, but it was elevated in the left eye. The presence of such deep glaucomatous cupping in the left eye is in favor of the assumption that the tension was temporarily even higher than that noted in the record. In the right fundus, which showed physiologic cupping, there were many retinal hemorrhages, caused by the obstruction of veins and the sclerotic condition of the arteries. In the left, or glaucomatous, eye no hemorrhages could be seen, although the vascular condition was apparently the same as that in the right eye.

Altogether, it appears that a high intraocular tension influences the extravasation into the retina and that retinopathy, such as albuminuric or diabetic retinitis, either diminishes or disappears when glaucoma develops or that such a retinopathy does not occur in an already glaucomatous eye. Of course further clinical experience is necessary to settle this point.

The logical corollary of such a concept is that a low intraocular tension produces a tendency to an especially pronounced extravasation from the retinal vessels, especially in cases of general hypertension. As far as I know, there do not exist statistics on intraocular tension in cases of retinopathy, but Dr Cogan with whom I discussed this problem, showed me a list of such cases, in which he had been called in consultation and in which he had tested the intraocular tension as a routine. It was interesting that in most of them—not in all—the intraocular pressure was surprisingly low.

#### RELATION OF HEMORRHAGIC OR NONHEMORRHAGIC CHARACTER OF VENOUS OBSTRUCTION TO INTRAOCULAR TENSION

Not much attention has so far been paid to the statement that the intraocular tension is generally low in cases of retinal venous thrombosis. Moore<sup>3</sup> stated that in all but 1 of his 13 cases of total obstruction tension was lower than that in the healthy eye. Wessely<sup>4</sup> confirmed this statement from his own experience, he noticed this difference also in cases of thrombosis of a tributary vein. Wessely stated that this decrease of tension was probably due to narrowing of the retinal and uveal arteries.

Development of the venous thrombosis has of course nothing to do with the lowered intraocular tension, the question is, however, whether the extravasation of blood is facilitated by the diminished pressure outside the vessel wall.

In this connection, it is interesting to compare anatomically verified cases of retinal venous obstruction in which, as usual, the obstruction was primary and the glaucoma secondary with cases in which glaucoma existed at first and the obstruction developed later.

In 1913 Verhoeff<sup>5</sup> studied the effect of chronic glaucoma (following occlusion of the pupil, corneal ulcer, anterior staphyloma, cataract extraction or serous iritis) on the central retinal vessels in 39 cases. He showed that in every case there was endovasculitis of the central vessels and that there was frequently, especially in the central vein, complete, or almost complete, obstruction. The changes in the central vessels were essentially the same as those which have been described in the literature and which Verhoeff himself had observed in association with hemorrhagic glaucoma. He stated

The almost complete absence of retinal hemorrhages in this series of cases is noteworthy. Thus, out of fifteen cases of complete or almost complete obstruction of the central vein, in only one case were they present in any significant number. In two other cases there were a few small hemorrhages, but it was doubtful if they were the result of the obstruction of the central vein.

Neither was edema of the retina prominent in any one case. According to Verhoeff, the infrequent occurrence of retinal hemorrhage was probably due, in some cases to the extensive

3 Moore, F. Retinal Venous Thrombosis. A Clinical Study of Sixty-Two Cases Followed over Many Years, London, George Pulman & Sons, Ltd, 1924.

4 Wessely, K. Ueber die Prognose der Thrombose der Centralvene, Klin Monatsbl f Augenh 95:398, 1935.

5 Verhoeff, F. H. The Effect of Chronic Glaucoma on the Central Vein Vessels, Arch Ophth 42:145, 1913.

involvement of the artery and in others to the slowness of the process, which allowed for the establishment of adequate collateral circulation.

An article by Salzmann<sup>6</sup> on "glaucoma and retinal circulation" to which I<sup>7</sup> referred in a previous paper, also has a relation to the topic under consideration. He studied the anatomic condition of the central vein and the retina in 80 eyes which were enucleated because of absolute glaucoma. In most cases the condition was of too long standing for one to evaluate which had come on first, the glaucoma or the venous obstruction. In a few cases, however, the sequence was fairly certain. In cases 42 and 43, patients with general hypertension had typical thrombosis of the central vein with numerous retinal hemorrhages and exudates and several weeks later glaucoma developed. In contrast to this usual course of events, there were other cases in which the glaucoma preceded venous obstruction. For example, in case 49 a woman aged 64 with glaucoma showed a severe and progressive visual disturbance four years after the appearance of glaucoma. Ophthalmoscopic inspection revealed tortuous veins in the area of deep glaucomatous cupping, but neither ophthalmoscopic nor histologic examination showed any hemorrhages or exudates in the retina. Autopsy revealed absolute obstruction of the central vein. In case 50 a man aged 64 had traumatic luxation of the lens with subsequent glaucoma. Enucleation was performed one year after the injury. Histologically, there were great changes in the venous vessels, especially in the superior retinal vein but no hemorrhages in the retina could be seen. Salzmann was in favor of the idea that the absence of hemorrhages was due to newly formed collaterals in the retina. Also, Scheerer<sup>8</sup> made two observations of interest in connection with this question. In his case 1 the glaucoma was primary and the thrombosis of the central vein secondary. The latter condition could be diagnosed only anatomically, after enucleation, for during life no retinal hemorrhages were visible. Case 4 was similar in this respect. But in case 14 there was glaucoma simplex, with eventual development of retinal hemorrhages. Enucleation was performed one year after the appearance of the ophthalmic trouble. Histologic study showed that the cen-

tral artery and the central vein were almost completely obstructed.

The studies of Verhoeff, Salzmann and Scheerer were made chiefly from an anatomic point of view, the clinical data given were generally brief, or the situation was so complicated that most of the cases could not be used in the present study. The observations mentioned, however, seem to support the view that intraocular pressure often has a bearing on the presence or absence of retinal hemorrhage. It may be added that Coats<sup>9</sup> in his exhaustive work on obstruction of the retinal vein, pointed out that in his experience the sequence of glaucoma first and obstruction of the retinal vein later is extremely rare. He encountered only 1 case, and that was doubtful. In Coats's opinion, only cases with retinal hemorrhages were recognized as full fledged instances of venous thrombosis. Thus he apparently missed the cases without hemorrhages.

In 1905, Harms<sup>10</sup> had stated "It is a well known fact that the opportunity of observing venous obstruction in an eye with primary glaucoma is rare."

#### PAPILLEDEMA AND HEMORRHAGES IN EYES WITH DECREASE OF INTRAOCULAR TENSION

Another condition undoubtedly related to lowering of the intraocular pressure must be discussed. This is the papilledema which occurs sometimes in eyes with very low pressure (after penetrating wounds or in disease), and which disappears when the intraocular tension becomes normal. It is thought to be of purely mechanical origin, like the papilledema associated with high intracranial pressure (Behr<sup>11</sup> Duke-Elder<sup>12</sup> and others). It could be proved anatomically that no inflammatory factor is involved. It is not easy to explain why such edema develops in the disk only, and why it occurs only in certain cases. The diminished ocular tension is apparently the most important, but not the only, etiologic factor. There is edema, but no hemorrhages or exudative patches probably because neither the content nor the walls of the vessels are pathologic. The transudation is facilitated by a vascular dilation, which follows the sudden fall of intraocular pressure. According

6 Salzmann, M. Glaukom und Netzhautzirkulation, Berlin, S. Karger, 1933.

7 Igersheimer, J. Ist ein Glaukom imstande die Transsudation aus den Netzhautgefäßen zu beeinflussen? *Ophthalmologica* **97** 146, 1939.

8 Scheerer, R. Zur pathologischen Anatomie der Veränderungen der Netzhautzentralgefäße bei der sogenannten Thrombose der Zentralvene und Embolie der Zentralarterie, *Arch f Ophth* **110** 292, 1922, **112** 206, 1923.

9 Coats, G. Der Verschluss der Zentralvene der Retina, *Arch f Ophth* **86** 340, 1913.

10 Harms, C. Anatomische Untersuchungen über Gefäßerkrankungen im Gebiete der Arteria und Vena centralis retinae, *Arch f Ophth* **61** 1, 1905.

11 Behr, C. Ueber die im Anschluss an perforierende Bulbusverletzungen auftretende Stauungspapille. *Klin Monatsbl f Augenh* **50** 56, 1912.

12 Duke-Elder, W. L. *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1941, vol. 3.

to Sobansky's studies, cited by Lauber,<sup>13</sup> the relation between the pressure in the retinal arteries and that in the retinal veins, seems undisturbed

Kyrieleis<sup>14</sup> stated that there is no doubt the papilledema in eyes with low intraocular pressure is mechanical, but that increased transudation through the vessel walls as a cause of the papilledema is of little importance, since under such circumstances diffuse edema of the retina would necessarily develop. His explanation is as follows: 1 The lymph fluid of the eye normally has some outflow into the optic disk, and this outflow is favored by intraocular pressure. If the intraocular tension is low, there will be stagnation of the lymph in the disk. 2 The normal tissue pressure in the optic nerve between the disk and the lamina cribrosa is determined by the blood pressure and the intracranial pressure from the intravaginal space. If the intraocular tension is low, the anterior part of the optic nerve may protrude like a hernia.

It is noteworthy, also, that under the reverse conditions, namely, acute inflammatory glaucoma, hyperemia with slight edema of the disk, sometimes combined with retinal hemorrhages, may occur. In my opinion the reason that this hyperemia and edema occur under such different circumstances, with especially low and with especially high intraocular pressure, is as follows. In the case of extreme hypotony the lowered pressure is primary and the papilledema secondary, whereas in the case of acute glaucoma the great influx of blood into the ocular vessels and the increased transudation are probably primary, with a resulting high intraocular tension. As will be remembered, Friedenwald,<sup>15</sup> in a histologic study of acute glaucoma, noted the presence in all cases of edema of the ciliary body, which pressed the iris toward the angle of the anterior chamber.

If the intraocular tension is high and the vessel walls are diseased and friable because of arteriosclerotic changes, sudden diminution of the pressure may have the tragic result of an uncontrollable hemorrhage, as is well known.

Only a short time ago, I found another statement in line with the concept under discussion. Parker<sup>16</sup> gave evidence of the fact that even

papilledema caused by increased intracranial pressure has some relation to the intraocular pressure. When both eyes have equal tension, papilledema develops to an equal degree in the two eyes, but if and when the tension in one eye is lower than that in the other eye, papilledema generally develops first in the eye with the lower tension. Still more impressive were experimental studies of Parker on dogs and monkeys. The intraocular tension of one eye was reduced by trephination. After recovery from the effects of the operation, a second ophthalmoscopic examination was made, and, again, the tension was recorded. Then artificial intracranial pressure was induced by different means on the side opposite the eye in which the tension had been reduced. Each time papilledema developed first in the eye with the reduced tension. Bordley<sup>17</sup> confirmed the clinical statement of Parker and added an interesting experience. In a case of tumor of the brain one eye suffered from glaucoma. In this glaucomatous eye choked disk did not develop.

#### PRESSURE OUTSIDE THE VESSEL WALL IN PHYSIOLOGY OF TRANSUDATION

Passage of fluid through the capillary wall is frequently discussed in general physiology. The extensive studies of Krogh and Lewis have shown that the capillary vessels are independently contractile. The permeability of the capillary wall varies within wide physiologic limits, at one moment the capillary walls in a given area may be almost totally impermeable to colloidal substances, and shortly afterward, under the influence of lack of oxygen or of some other stimulus, the permeability may be greatly increased, so that blood plasma escapes readily into the tissue spaces. Such a change in permeability is characteristic of capillaries, whereas it is absent in arteries (Ebbecke<sup>18</sup>). Vasodilation increases, and vasoconstriction reduces, capillary permeability. According to Landis,<sup>19</sup> important factors controlling the movement of fluid through a membrane are as follows: (1) total area of filtering surface available, (2) properties, particularly permeability, of the membrane itself, and (3) pressures exerted on the fluids inside and outside the membrane.

13 Lauber, H. The Formation of Papilledema, *Arch Ophth* **13** 733 (May) 1935

14 Kyrieleis, W. Ueber Stauungspapille, *Arch f Ophth* **121** 560, 1929

15 Friedenwald, J. S. The Pathogenesis of Acute Glaucoma. Clinical and Pathologic Study, *Arch Ophth* **3** 560 (May) 1930

16 Parker, W. R. (a) The Relation of Choked Disk to Intraocular Tension. A Clinical Study of Six Cases, *Ann Ophth* **20** 715, 1911, (b) The Relation of Choked Disk to the Tension of the Eye, *J A M A*

**67** 1053 (Oct 7) 1916, (c) The Mechanics of Papilledema, *Tr Am Acad Ophth* **29** 77, 1924, (d) The Relation of the Tension of the Eyeball to the First Appearance of Papilledema, *A Research Nerv & Ment Dis*, *Proc* **8** 256, 1929

17 Bordley, J., in discussion on Parker,<sup>16b</sup> p 1056  
18 Ebbecke, U. Gefassreaktionen, *Ergebn d Physiol* **20** 401, 1923

19 Landis, E. M. The Passage of Fluid Through the Capillary Wall, in *Harvey Lectures, 1936-1937*, Baltimore, Williams & Wilkins Company, 1937, p 70

The permeability of the vessel wall, the blood pressure and the osmotic pressure are thought to be the principal factors in such a transudative process. The pressure outside the vessel wall is not often mentioned, for generally the circumstances are such that it does not play a great role. Edema, especially the experimental wheal, is the phenomenon by which the migration of fluid through the vessel wall has been chiefly studied experimentally. In these studies it was proved that the pressure outside the vessel wall may be of significance. Before the wheal itself develops, there is capillary dilation, the necessary increase of capillary permeability does not occur without such a dilation. If a wheal develops quickly, the capillary dilation will be counteracted by the pressure of the edema (Ebbecke<sup>18</sup>). Lewis,<sup>20</sup> in his experimental studies on vascular reactions, stated that the wheal normally following a heavy stroke may be prevented by pressure from outside, such as that exerted by an armlet. When a small wheal develops under a pressure capsule, it is small because the outside pressure checks the rate of blood flow in the affected vessels. In his Harvey Lecture, Landis<sup>19</sup> came to the following conclusions:

Apparently extravascular fluid distends the tissue spaces by developing a tissue pressure which at the same time diminishes progressively the effectiveness of a given capillary pressure in producing further filtration. The physiological importance of this tissue pressure is probably considerable.

The same author, in summarizing the factors concerned in the pathogenesis of edema, differentiated primary factors favoring formation of edema, such as elevated capillary pressure, lowered osmotic pressure to colloids, damage to the capillary wall and lymphatic obstruction, and contributory factors. The most important contributory factor is, according to Landis, a low tissue pressure, but he added

though the resistance of the tissues can delay, it cannot prevent the appearance of edema when venous congestion, capillary damage, or reduced colloid osmotic pressure favor filtration continuously over long periods of time.

#### COMMENT

From this brief excursion into general physiology, it can be seen that the pressure outside the vessel wall is recognized as a factor which may influence the transudation through the wall. Low external pressure favors, and high external pressure reduces or hinders, the transudation. Generally this factor does not play a great role, because there rarely occurs a condition in which pressure outside the vessels becomes very high

and localized, unless applied artificially by an armlet or other means. The situation is, of course, different in closed capsules, like the eyeball or the skull.

It is old knowledge that sudden lowering of the intraocular tension is often followed by dilation of the intraocular vessels, and even by a severe hemorrhage, if the vessel walls are abnormally permeable. The intraocular pressure, which is of course the pressure outside the vessel wall, seems to be of greater importance for the transudative mechanism in general than has hitherto been thought. If further studies confirm the aforementioned experiences, it will be established that intraocular tension influences the development and the type of exudation occurring with retinopathies. Low tension seems to facilitate such exudation, while glaucoma may reduce its extent, prevent it or cause the exudate to disappear entirely. Similarly, the hemorrhages associated with obstruction of a retinal vein generally occur in an eye with low tension and may be entirely absent in a primarily glaucomatous eye, even though the retinal vein is completely obstructed. It is interesting that the papilledema, in its development and sometimes in its degree, is also influenced by the intraocular pressure. This is valid not only for papilledema caused by intraocular hypotonic conditions (penetrating wound, iridocyclitis) but for the papilledema following increased intracranial pressure (Parker). Glaucoma prevented the development of papilledema in a case of cerebral tumor (Bordley). In retinopathy, as well as in thrombosis of the central vein, the situation is of course often complicated by a high arterial and capillary pressure, by a change in the protein content of the blood and by pathologic changes in the vessel wall. Thus, it would not be surprising if a high intraocular tension is sometimes insufficient to counteract transudation. Landis expressed similar views concerning the limitations of tissue pressure when other factors are too powerful.

Altogether, it seems of interest that clinical pictures which are so different in their origin and clinical aspects as retinopathies, venous obstruction and papilledema may have one factor in common, namely, that of being influenced by the intraocular pressure. It is interesting, also, that clinical ophthalmologic facts confirm the physiologically recognized significance which the external pressure has in the passage of contents of the blood through vessel walls, and that perhaps nowhere in the body are the conditions for proving this significance so ideal as in the globe.

Whether this whole concept can be utilized practically is a question for the future.

<sup>20</sup> Lewis, T. Vascular Reactions of the Skin to Injury, *Heart* 11: 119, 1924.

## SUMMARY

It is well known that the hydrostatic pressure, as well as the condition of the capillaries (constriction, dilation and permeability of the wall), the content of the blood and the resistance to the outflow of blood and lymph from the globe are the main factors which, if pathologically altered, may produce an increased passage of fluids and corpuscles through the vessel walls of the retina. It was not realized until now that, besides these factors, the intraocular pres-

sure seems to play a certain role in these transudative phenomena. A low tension facilitates transudation, a high tension may prevent exudation in eyes predisposed to retinopathy or in cases of obstruction of retinal veins. Such phenomena in the eyeball serve as especially good evidence for the general physiologic assumption that the pressure outside the vessel wall is of significance for the passage of fluid through the capillary wall.

636 Beacon Street



# DEFECTS IN VISUAL FIELDS PRODUCED BY HYALINE BODIES IN THE OPTIC DISKS

C WILBUR RUCKER, M D

ROCHESTER, MINN

The presence of hyaline bodies in the optic disks occasionally produces an appearance that may simulate that of chronic papilledema with secondary optic nerve atrophy. When the glistening bodies are large and lie near the surface, they cause little difficulty in diagnosis, but when they are small and lie buried so deeply within

was mentioned by Reese<sup>1</sup> in his excellent review of the subject in 1940.

In general, however, little attention has been paid to the associated visual defects, therefore, a consideration of this phase of the subject appears to be timely. I have reviewed the cases that I have seen during the past few years, and from

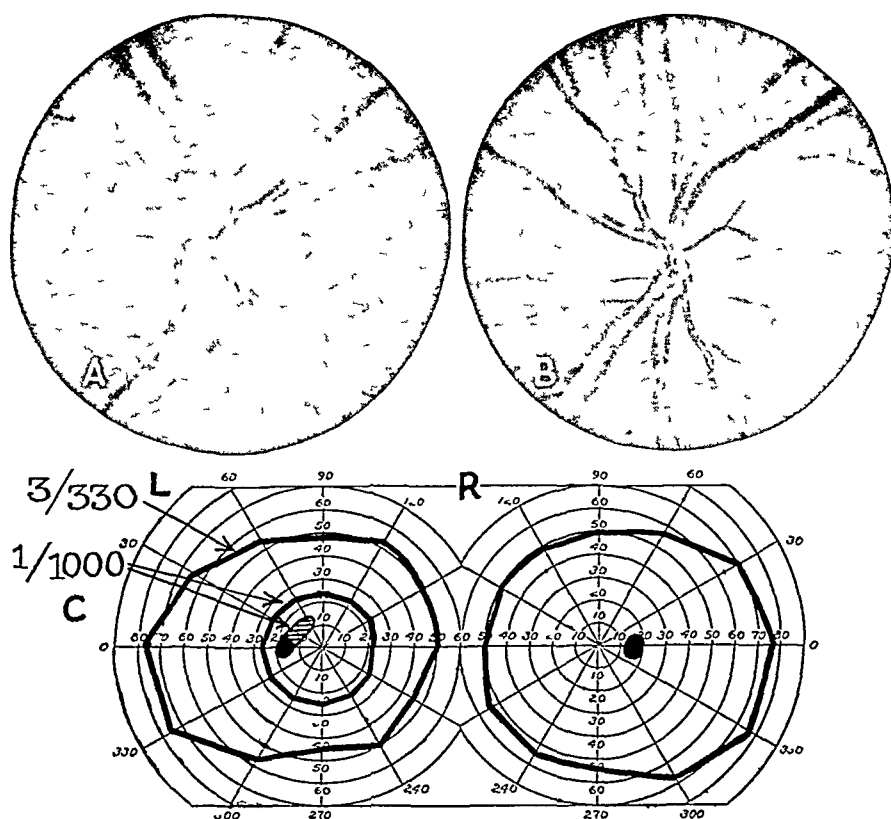


Fig 1 (case 1) —(A) right fundus, (B) left fundus, (C) visual fields. Vision was 6/10 in each eye.

the nerve substance that they are scarcely visible, they may cause a fulness that is difficult to explain. In fact, unless they are looked for specifically, they may pass unnoticed.

Not only is the appearance of the optic disks misleading, but field defects are encountered rather frequently in this condition, either in the form of peculiar contractions or of arcuate scotomas. Such defects may confuse the diagnostician still further. This impairment of vision

the group in which the perimetric fields were plotted I have selected a few diverse types. They largely demonstrate how variable may be the defects.

## REPORT OF CASES

CASE 1 —A woman aged 29 complained of nervousness, increased appetite and loss of weight. These were found to be due to exophthalmic goiter, and subtotal thyroidectomy was performed. There were no symptoms refer-

1 Reese, A. B. Relation of Drusen of the Optic Nerve to Tuberculous Sclerosis, Arch Ophth 24 187-205 (July) 1940.

From the Section on Ophthalmology, the Mayo Clinic.

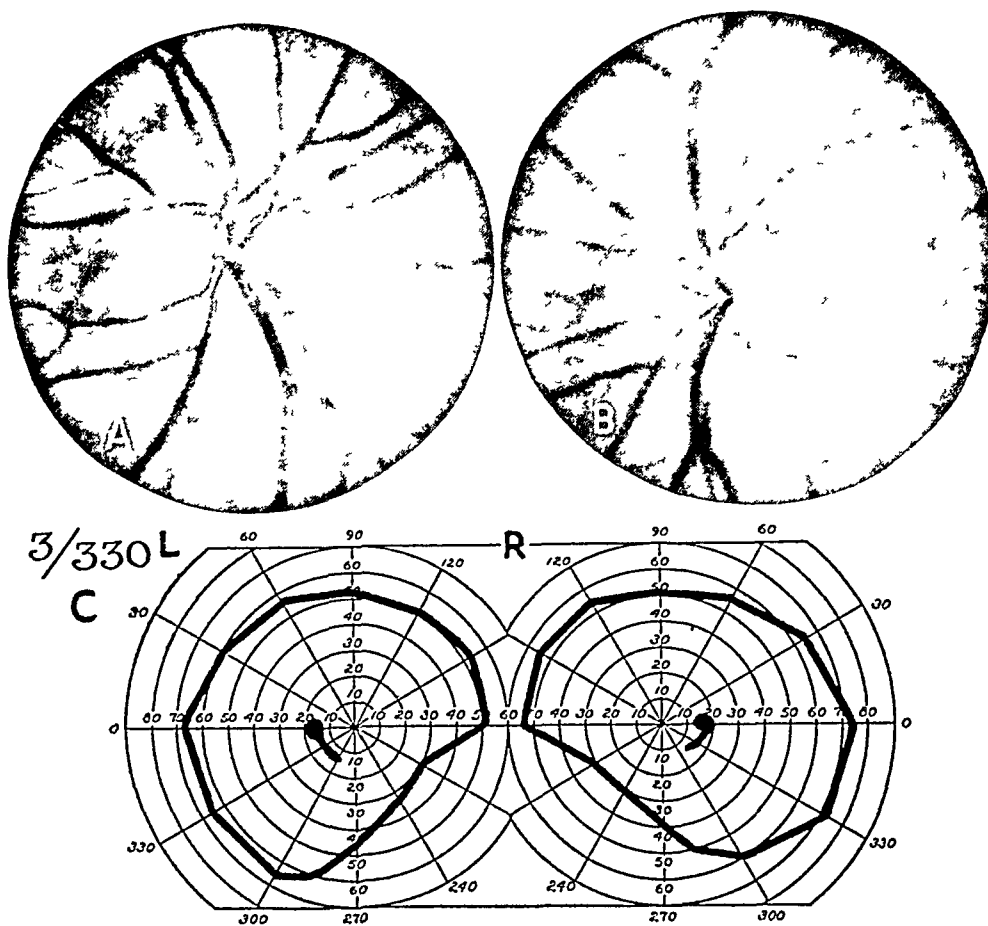


Fig 2 (case 2) —(A) right fundus, (B) left fundus, (C) visual fields Vision was 6/6 in the right eye and 6/10 in the left eye

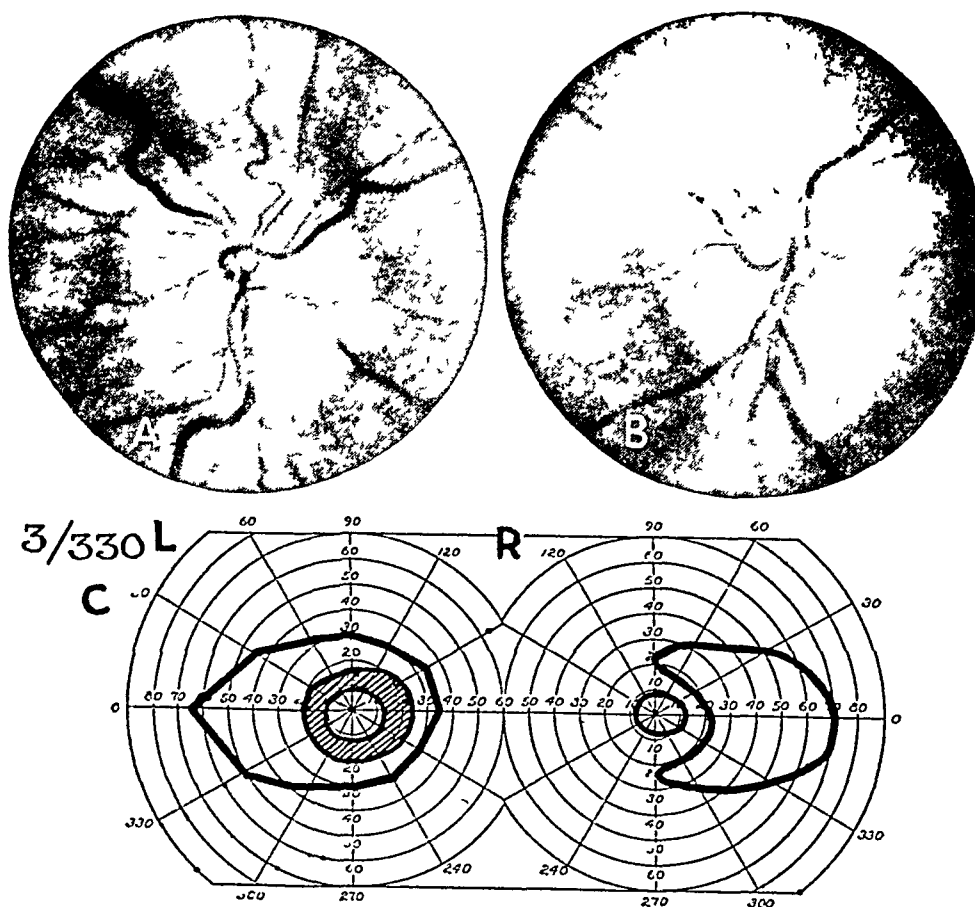


Fig 3 (case 3) —(A) right fundus, (B) left fundus, (C) visual fields Vision was 6/7 in the right eye and 6/10 in the left eye

able to the eyes. Neurologic examination was not performed.

Ophthalmoscopic examination disclosed large hyaline masses in both optic disks. The right was elevated 2 D and the left 1 D (fig 1 A and B).

When the visual fields were plotted, it was found that the normal blindspot of the right eye was enlarged and that a small arcuate scotoma extended upward from the blindspot of the left eye (fig 1 C).

of the pain, and abdominal hysterectomy was performed. Neurologic examination disclosed no abnormalities except absence of deep tendon reflexes in the legs. There were no visual symptoms.

On ophthalmoscopic examination, hyaline masses were seen on both optic disks, the right disk was elevated 2 D and the left 1 D (fig 3 A and B).

Plotting of the fields of vision disclosed a dense ring scotoma in the field of the left eye and a similar ring,

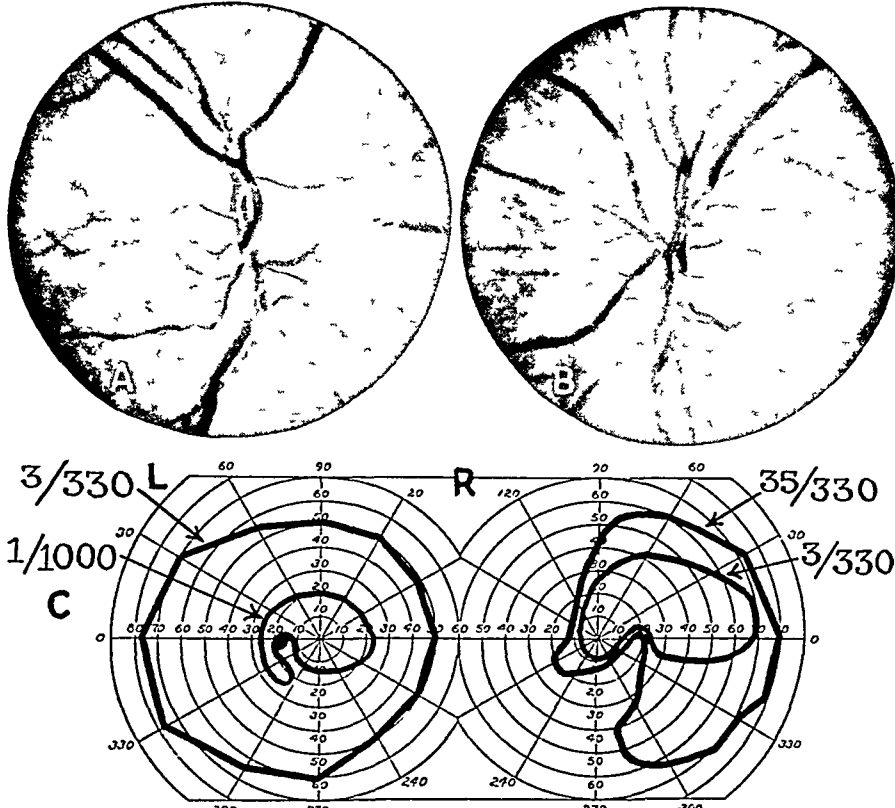


Fig 4 (case 4) —(A) right fundus, (B) left fundus, (C) visual fields. Vision was 6/7 in the right eye and 6/6 in the left eye.

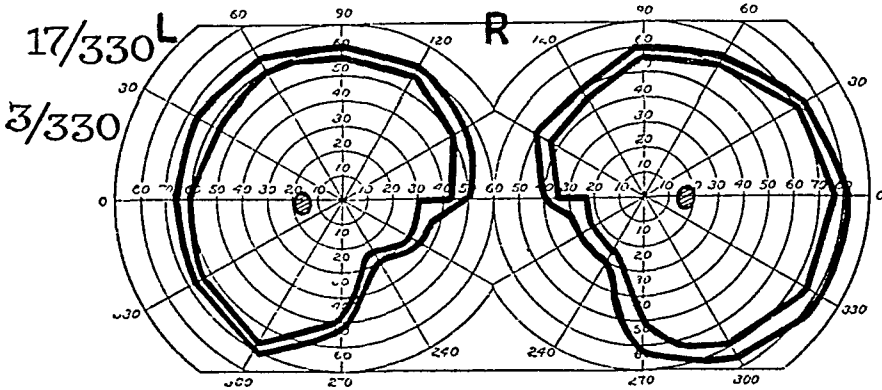


Fig 5 (case 5) —Visual fields. Vision was 6/6 in each eye.

**CASE 2**—A woman aged 46 complained of headaches. For many years they had occurred every few months, but had become more frequent during the past four years and constant for the past four months. The neurologic diagnosis was “involutional change in migraine.”

On both optic disks there were piles of hyaline bodies (fig 2 A and B).

Plotting of the visual fields revealed binasal contraction and small, dense arcuate scotomas pointing downward (fig 2 C).

**CASE 3**—A woman aged 49 complained of pain in the back. Large uterine fibroids were found to be the cause

which had broken through to the nasal periphery, in the field of the right eye (fig 3 C).

**CASE 4**—A man aged 39 complained of headache of six weeks’ duration. His family physician had plotted his visual fields and, on finding a defect, had urged him to go to a large clinic for neurologic and ophthalmic examinations.

Ophthalmoscopic examination of the right optic disk disclosed several hyaline bodies, which gave it a pale color, and at the nasal margin of the left disk there were two deep bodies of a similar nature (fig 4 A and B).

The visual fields contained arcuate scotomas, the one in the right eye had broken through to the nasal periphery (fig 4 C)

CASE 5—A girl aged 15 years had consulted her local oculist because for a year she had been having occasional headaches and thought she might need glasses. On examination of her eyegrounds, he suspected the presence of chronic papilledema, and his suspicion was not allayed when he plotted the visual fields and found binasal contraction. Because of these findings, he asked her to seek further advice at a large clinic. Extensive clinical and laboratory tests and a neurologic examination failed to disclose any abnormalities.

Many hyaline bodies were seen in the optic disks on ophthalmoscopic examination. The fundi were not photographed.

Binasal contraction was demonstrated by plotting the visual fields (fig 5).

#### COMMENT

These cases illustrate the usual varieties of defects in the visual fields caused by hyaline bodies on the optic disks. There may be enlargement of the normal blindspots and arcuate scotomas, either in the form of small fingers or of large arms breaking through to the periphery, or there may be peripheral contraction, which most often is below and on the nasal side.

# TUBEROUS SCLEROSIS ASSOCIATED WITH TUMOR OF THE OPTIC DISK (PHACOMA)

MAJOR EARL A GLICKLICH, MAJOR ABRAHAM SCHULTZ

AND

COLONEL JULIEN E BENJAMIN

MEDICAL CORPS, ARMY OF THE UNITED STATES

We are reporting a case of tuberous sclerosis with the characteristic syndrome of adenoma sebaceum, epilepsy and mental deficiency, associated with tumor of the optic disk (phacoma)

## REPORT OF CASE

*History*—An American soldier aged 22, unmarried, was first seen in December 1942. He was admitted from an overseas hospital with a transfer diagnosis of tuberous sclerosis and epilepsy of the grand mal form.

The patient had been inducted into the Army on Feb 10, 1942 at Fort Bragg, N C. Several weeks later he had had an epileptiform seizure from which he promptly recovered. In March 1942 he had pneumonia, for which he was hospitalized one month.

He was sent overseas in July 1942. He felt well except for a residual dry cough which had persisted since the attack of pneumonia. The cough became more frequent at night, although it was nonproductive. On Aug 28, 1942 the patient was admitted to an overseas hospital because the cough had become progressively worse. During hospitalization the cough improved. On further investigation of his epileptiform seizures, it was suspected that this patient had tuberous sclerosis, as manifested by a familial history of epilepsy and the presence of cutaneous lesions and of vestiges of congenital anomalies. The patient was therefore returned to the United States for further observation and treatment.

The patient was born April 28, 1919. He was a full term baby and had a normal birth. He talked early, walked at the age of 14 months and teethed at normal age. He had measles, mumps and whooping cough in childhood. He entered school when he was 7 years old and completed the fourth grade at the age of 14. He learned to read and write but never learned arithmetic. In his youth he worked on farms with his parents, where he was able to perform simple chores.

His first epileptiform seizure occurred at the age of 7, and since then he had had four similar attacks. The last seizure occurred shortly after induction, as previously mentioned. The patient stated that the onset of these seizures was preceded by dizzy sensation and loss of vision, followed by loss of consciousness. On regaining consciousness he noted weakness and nausea, after which he fell into a deep sleep. The patient did not recall biting his tongue or injuring himself during any of these seizures.

*Family History*—Investigation of the family by the Red Cross revealed that the father was 63 years old and slightly deaf. He had high blood pressure and had a cutaneous condition similar to that present in the son, involving the face and nose. He impressed one as being hopelessly limited both physically and mentally. The mother was 60 years old and presented no cutaneous changes. She showed more initiative than the husband, though she was illiterate. Two sisters of the patient

were living and well. One of the sisters had a condition of the skin of the face similar to that of the patient. The patient had four brothers, of whom only the oldest was living. He was 39 years old, had had epilepsy for four years as a child and also had cutaneous lesions on the face resembling those of the patient. He had not gone beyond the third grade of grammar school. He had been crippled in an accident and appeared to be definitely mentally retarded. Three brothers had died, one at the age of 10 months, of colitis, another at the age of 3 years, of pneumonia and the third at the age of 20 years, of undetermined cause. The last-mentioned brother, who had not advanced beyond the second grade of grammar school, had had epileptic attacks which started at the age of 4 years and continued until his death. He was always an invalid and was considered to be of low mentality.

*Physical Examination*—The patient was 70 inches (178 cm) in height, weighed 165 pounds (74.8 Kg) and did not appear acutely ill. The pharynx and teeth were normal. There was no significant adenopathy. Examination of the heart, lungs and abdomen revealed no abnormal conditions. Neurologic examination gave essentially normal results. The blood pressure was 110 mm systolic and 70 mm diastolic.

*Dermatologic Examination*—Definite lesions of adenoma sebaceum (fig 1) were present on the face, being characterized by areas the size of a pinhead to that of a split pea distributed over the nose, cheeks and nasolabial folds. The lesions were yellowish and pinkish, discrete, soft and moderately compressible, and the superficial capillaries in the affected region were generally telangiectatic. A hard, whitish cystic growth was present just below the right internal canthus. Similar lesions were also present behind the ears. The skin of the trunk and extremities was normal in appearance and texture.

*Ocular Examination*—The patient had no symptoms referable to his eyes. Vision was 20/20 in each eye, and small print could be read with ease. The eyes were essentially normal with the exception of the right fundus. In the latter an oval, glittering, gray mulberry-like growth occupied the inner half of the disk and projected over its nasal margin. The mass was elevated 2 diopters. The surface of the lesion consisted of closely packed nodular cysts, over which the retinal vessels coursed. A small, superficial, striated area of hemorrhage was present near the inferior pole of the tumor (fig 2). The visual fields were normal except for an enlargement of the physiologic blindspot in the right eye, which was extended temporally to twice the normal size.

*Mental Examination*—The patient was orderly, friendly and cooperative. His speech was spontaneous, coherent and relevant. His mood was normal, and no

delusions or hallucinations were present, but he was only partially oriented. A Kent emergency test gave an intelligence quotient of about 65. The Stanford-Binet formal test revealed a quotient of 70 and a mental age of 11 years and 2 months. The clinical impression of the psychiatrist was that the patient was a borderline mentally defective person with defects most evident in the fields of memory, retention and recall.

*Laboratory Examination*—The sedimentation rate, the serologic reactions of the blood, the amount of

long bones with the exception of an old ununited fracture of the right ulnar styloid process. Intravenous and retrograde pyelography revealed no abnormal conditions.

*Histologic Examination of Skin* (Made by Lieut Col Robert Fienberg)—Numerous small and large sebaceous glands were found in the corium. No true neoplasia was evident. The ducts were dilated and filled with keratin. A few dilated blood vessels were seen. Scattered lymphocytes were present in the corium,

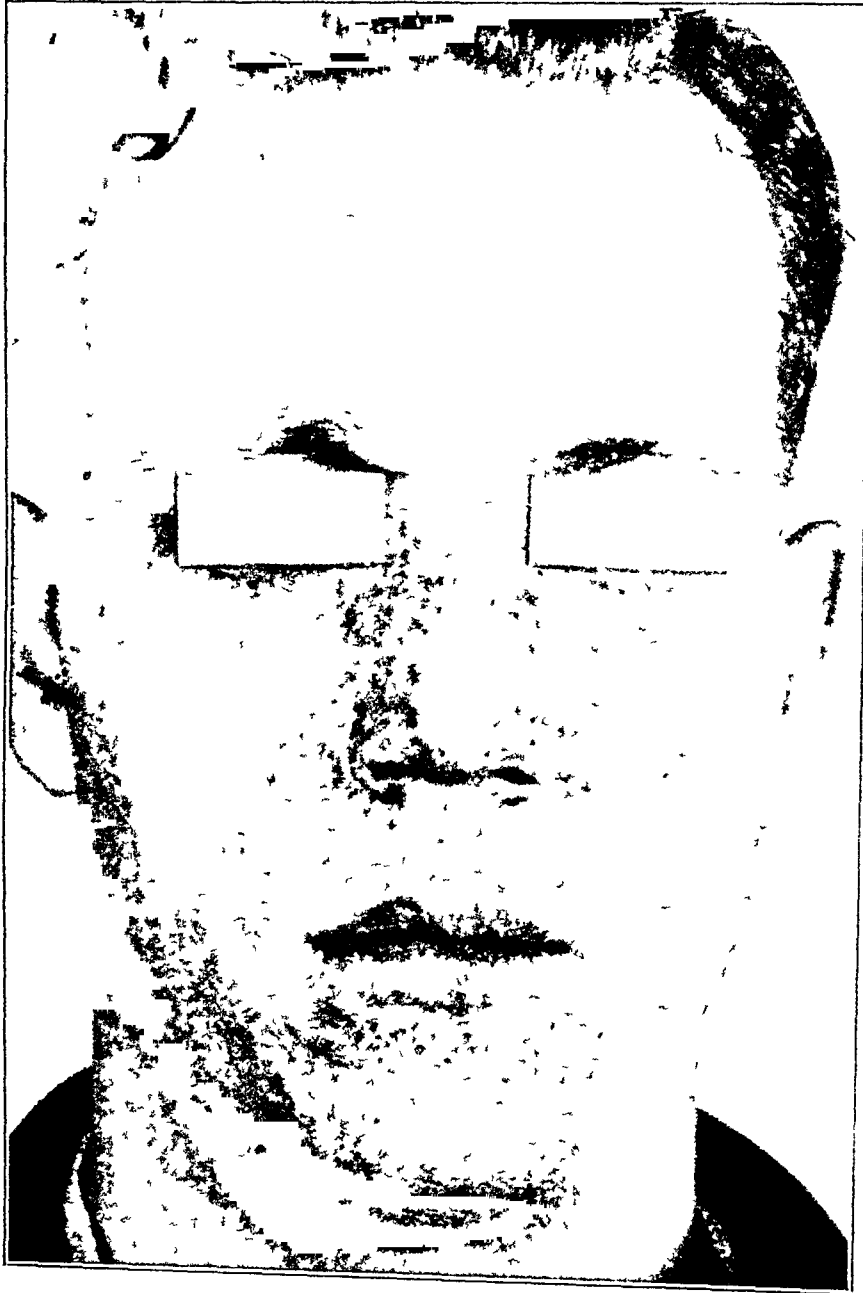


Fig 1—Photograph of a patient with tuberous sclerosis showing the associated cutaneous lesions

nonprotein nitrogen in the blood, the sputum, and the cellular elements of the blood (by complete blood count) were all within normal limits, except the leukocytes, which were slightly increased in number. The urine contained numerous white and red blood cells, with occasional hyaline casts, on several occasions.

*Roentgenographic Observations*—Roentgen examination of the chest revealed no abnormality of the heart or lungs. The calvarium was of average thickness. No evidence of abnormal calcification was present. The sella turcica appeared normal, and the pineal calcification occupied its usual position. An encephalogram revealed slightly dilated ventricles with irregularities of their walls. No abnormalities were noted in the

and a few pigmented phagocytes were present just below the basal cells of the epithelium.

*Course in the Hospital*—No epileptiform seizures were observed during the period of hospitalization. It was established that the syndrome of tuberous sclerosis, comprising mental deficiency, epilepsy and adenoma sebaceum, was present in the patient. In addition, a tumor of the optic disk was present in the right fundus. It was suspected that tumors were also present in the ventricles of the brain because of the conditions described in the report on an encephalogram from the overseas hospital. Renal involvement was suspected because of the numerous red and white cells occasionally present in the urine, though retrograde and intravenous pyelo-

grams revealed no abnormality. Because of the conditions discovered the patient was separated from the military service and escorted home.

#### COMMENT

Adenoma sebaceum is one of the cutaneous manifestations associated with the syndrome known as tuberous sclerosis. The other manifestations of the disease are epilepsy and low grade mentality. Evidence of the condition is usually present in one or more members of the family. Autopsy reveals interesting changes in the brain in the nature of nodular sclerosis of the cerebral cortex with hard, tiny, potato-like tumors, from which the name of the condition is derived. Other congenital anomalies have been reported involving various organs, such as the kidneys, heart, liver, gastrointestinal tract and retina. The association of epilepsy with this

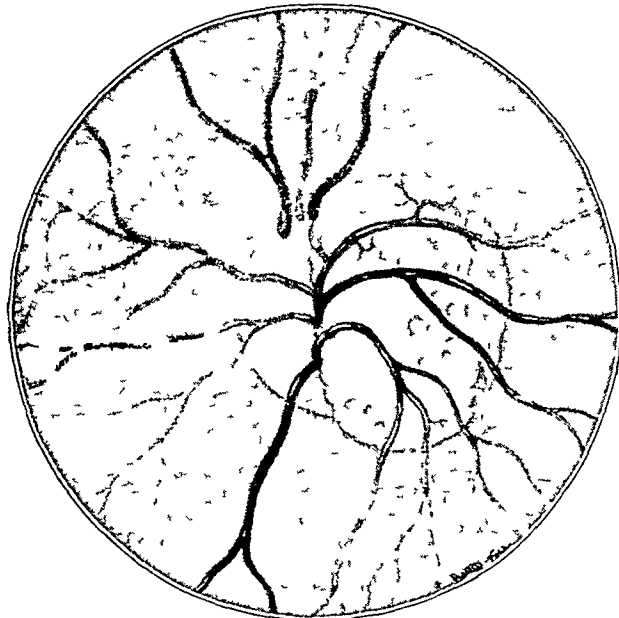


Fig 2—Drawing of the right fundus showing the tumor of the optic disk (Miss Betty Foss, of the Massachusetts Eye and Ear Infirmary, made this drawing.)

condition is of interest. It is possible that in many cases of "idiopathic epilepsy" tuberous sclerosis is the pathologic basis.

Phacoma of the optic disk is particularly interesting in this case because of the extreme rarity of reports of this condition in the American literature. Though Bourneville had already established the syndrome of tuberous sclerosis in 1880, the associated retinal lesions were not recognized until 1921, when van der Hoeve<sup>1</sup> first described them in reports on 6 patients suffering from this disease. He called the lesions *Phakomata* from the Greek word *phakos*, meaning "mother spot," believing that they arose from embryonic cell rests. Since then relatively few retinal tumors have been described. Critchley

and Earl<sup>2</sup> found only 1 phacoma in their series of 29 cases of tuberous sclerosis. In a comprehensive review of the literature by Messinger and Clarke<sup>3</sup> 18 more cases of retinal tumors in tuberous sclerosis were added. In 5 of the cases there were phacomata of the optic disk as well as the retina. To this group the authors added their own case of tumor of the nerve head with descriptions of the ophthalmoscopic and histologic observations. Other instances of phacoma of the retina have been described by Gifford,<sup>4</sup> Bloch and Grove<sup>5</sup> and Koch and Walsh.<sup>6</sup> On the basis of retinal changes Givner<sup>7</sup> diagnosed tuberous sclerosis in a 5 month old infant with convulsions. The diagnosis was subsequently confirmed by an encephalogram which showed the "candle droppings" of the ventricle.

Though phacomata occur less frequently in tuberous sclerosis than the cutaneous lesions or the mental changes, it must be remembered that changes in the fundus may sometimes be the sole manifestation of this syndrome. Under such circumstances tuberous sclerosis must be differentiated from the allied conditions in which retinal phacomata occur. These conditions include (1) von Recklinghausen's neurofibromatosis, which affects the skin and cranial nerves, (2) von Hippel's retinal and Lindau's cerebral angiomas, (3) Sturge-Weber's syndrome (angiomas cerebri), characterized by buphthalmos, enlargement of the cerebral vessels and nevus flammeus, and (4) retinal glioma in infants. The changes in the fundus in tuberous sclerosis are polymorphic, the phacomata may be single or multiple, flat or raised, and there may be various pigmentary changes in the retina. About one fifth of the retinal phacomata are confined to the optic disk, as in this case. The most typical lesion is an elevated, gray, mulberry-like growth, such as was present in the fundus of this patient.

The origin of tumors of this type is still not certain, though they are generally recognized to be primarily ectodermal malformations, consisting of glial tissue and undifferentiated elements, including mesoderm, initiated by developmental and hereditary factors.

2 Critchley, M., and Earl, C. J. C. Tuberous Sclerosis and Allied Conditions, *Brain* **55** 311 (Sept.) 1932.

3 Messinger, H. C., and Clarke, B. E. Retinal Tumors in Tuberous Sclerosis. Review of Literature and Report of a Case, *Arch Ophth* **18** 1 (July) 1937.

4 Gifford, S. R. Phakoma Retinae and Adenoma Sebaceum, *Arch Ophth* **24** 967 (Nov.) 1940.

5 Bloch, F. J., and Grove, B. A. Tuberous Sclerosis with Retinal Tumor, *Arch Ophth* **19** 34 (Jan.) 1938.

6 Koch, F. L. P., and Walsh, M. N. Syndrome of Tuberous Sclerosis, *Arch Ophth* **21** 465 (March) 1939.

7 Givner, I. Ophthalmologic Aids in Neurologic Diagnosis, *Arch Neurol & Psychiat* **47** 1067 (June) 1942.

1 van der Hoeve, J. Retinal Tumors in Tuberous Sclerosis, *Arch f Ophth* **105** 880, 1921.

# CHALCOSIS LENTIS ASSOCIATED WITH TRAUMATIC LENTICONUS POSTERIOR

CAPTAIN EMANUEL ROSEN

MEDICAL CORPS, ARMY OF THE UNITED STATES

The chemical reaction of copper in the lens is one of the few ophthalmologic subjects which has not been overemphasized in the literature. Chalcosis lentis has been encountered frequently during the present war because of the employment of numerous alloys in armaments, some of which contain copper. The toxicity of copper within the globe is well known, and the production of a characteristic "sunflower" just below the anterior capsule of the lens has been regarded as one of the pathognomonic signs of chalcosis lentis<sup>1</sup>. The presence of the "sunflower" is frequently difficult to determine, and certain methods of examination should be employed to bring out this outstanding characteristic. A "sunflower" has been reported by Thiel as occurring in cases of hepatolenticular degeneration, but this lesion has not the appearance or the color of that associated with chalcosis lentis.

Since the "sunflower" occurs in the region of the lens just below the anterior capsule, and since the lens usually shows opacification at various depths as the result of penetration of the foreign body, it is necessary so to direct the beam of light of the slit lamp that it does not penetrate to the more posterior opacities of the lens. The focal beam of light must be brought in from an extremely temporal position, with the pupil widely dilated. In this manner, the ray of light will strike over the anterior capsule only and will not pass into the other layers of the lens. If the rays of light strike more deeply into the lens, the opacities existing in the depths of the lens will be rendered visible, and the great play of light on these opacifications will be so intense that the more anterior, and less opaque, "sunflower" will

become invisible. The character of the "sunflower" is such that when there is an opacity posterior to it, its morphologic features cannot be recognized either by focal illumination or by retroillumination.

When the beam from the slit lamp is brought in from the extreme temporal side and the "sunflower" is viewed through the microscope, approximately the nasal half can be seen. This is due to the fact that the dilated and thickened iris acts as a barrier so that the light does not reach the temporal half of the anterior capsule. If the angle of incidence is made more acute, more of the temporal portion of the anterior capsule may be seen, but as the light passes from the temporal to the nasal side, the thin zone of the "sunflower" is by-passed, the nasal portion of the "sunflower" becoming visible.

## REPORT OF A CASE

An Army private aged 19 stated that in December 1942, while he was still a civilian, a 22 mm rifle with which he was practicing accidentally "backfired" and exploded directly into his eye. It is assumed that the patient failed to close his eye at the moment of "backfire," for the injury was direct to the eyeball. Several small copper particles were removed by the nurse, for the family physician was not available at the time of injury. However, when the patient returned the next day, his physician recommended that he use an ointment and drops several times daily. One week later, because the eye had failed to respond to this treatment, the patient consulted an ophthalmologist, who removed many residual fragments from the right cornea. The pupil was dilated, and the patient was told that deeply embedded foreign bodies were still present in the cornea and that they had better be left alone. No mention was made of the penetration of any particles through the cornea or of the presence of any intraocular foreign elements. Three weeks later, when the patient returned to the ophthalmologist, vision was as good in the right eye as it was in the left eye.

About one week later, while playing basketball, the patient was jabbed in the right eye by a finger of one of the players. The eye became painful and blurred soon after this incident, but since the patient had been told not to return to his physician for three weeks, he followed this direction literally. On the occasion of his next visit, the patient was told that the second injury was much more serious than the first and that a "film" had now formed on the eye. The patient returned to this physician several times and eventually was advised that the eye would improve. On May 22, 1943 he was inducted into the Army, with a visual record of 20/40.

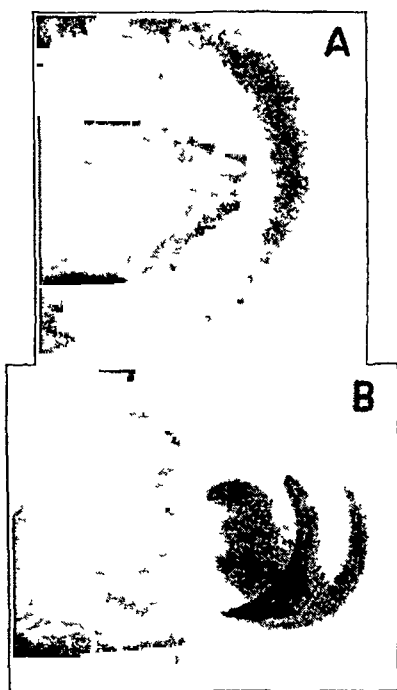
1 Cordes, F. C., and Harrington, D. O. Bilateral Absorption of Intraocular Copper with Chalcosis in One Eye, *Am J Ophth* **18** 348, 1935. Coppez, H. Sur la chalcose oculaire, *Arch d'opht* **45** 609, 1928. Ertl, F. Fremdkorper (Kupfersplitter) im Glaskorper, *Centralbl f prakt Augenh* **31** 322, 1907. Weiss, W. Zur Entstehung der Verkupferung des Auges durch intraokulare Kupfersplitter, *Arch f Ophth* **117** 114, 1926. Sala, G. Sulla calcosi oculare con particolare riguardo all'aspetto biomicroscopico della cataratta da rame, *Boll d'ocul* **13** 1047, 1934.



for his right eye. A letter subsequently received from the aforementioned ophthalmologist stated that "several particles of powder and corneal scars were of negligible importance. The serious involvement was plastic iritis, secondary to injury from a finger nail."

The patient was admitted to the ophthalmic service of the station hospital, where several interesting observations were made.

1 Vision on admission was 20/70 in the right eye and 20/20 in the left eye. There was no apparent involvement of the adnexia, and the conjunctiva of neither eye showed injection. Muscle balance was normal in all the cardinal directions of gaze, with the near point of convergence 95 mm. On the temporal side of the bulbar conjunctiva of the right eye two small foreign bodies were embedded just beneath the conjunctiva. The cornea showed several areas of scar formation and some areas in which metallic foreign bodies were still deeply embedded in the cornea. One small foreign body, extending horizontally across the cornea for a distance of 2 mm on a level with the



A, "glass tubings," visible just behind the posterior bulge, B, nasal half of the "sunflower," seen with the slit lamp at a wide angle of incidence.

lower border of the pupil, had the distinctive color of copper. Just above this was a small, opaque corneal scar, located at about 9 o'clock, but about 3 mm within the limbus. This was the most important corneal disturbance, being the opacity produced by the penetrating foreign body. When the narrow beam of the slit lamp was passed through this opacity, the penetrating nature of the corneal scar could be determined. At the endothelial terminus of the corneal scar a small indentation could be seen, breaking up the parallelism of the corneal beam.

2 There was no cellular deposit in the anterior chamber and no evidence of recent or old iritis. The zone of specular reflection, playing off the endothelial surface of the cornea, failed to show any "crater formation," and no disturbance was noticed in the endothelial "mosaic" except in the region of penetration of the corneal injury described in the preceding paragraph.

Following an angle of about 25 degrees with the visual axis, a rhomboid defect was seen in the iris at about the region of the "collarette," at 9 o'clock. The color of the iris in the injured eye was similar to that of the iris of the left eye.

When the pupil was dilated and the same angle followed (which represented the trajectory of the intraocular missile), a dense, irregularly circular opacity was seen on the anterior capsule. This lesion was superficial, grayish white and imbricated. This opacity did not extend below the surface of the lens.

3 With the narrow beam of the slit lamp passing through the various layers of the lens, many interesting changes were noted. Just below the reduplication line of the anterior capsule was a row of dotlike, bluish green opacities, in parallel arrangement, filling the entire section of the corneal beam and extending from the upper to the lower border of the iris. As the thickness of the corneal beam was increased, these minute dots could be seen to be part of the "sunflower."

When the "sunflower" was viewed with the diffuse beam of light from the extreme temporal side, the exact size of the lesion could be determined. It consisted of an inner circle, 2.5 mm in diameter, containing an almost optically empty center. Radiating from this ring were several narrow "petals," of variable length and microscopically made up of small, round, isolated dots, so closely packed together that the entire structure seemed homogeneous. The "sunflower" was aquamarine under focal illumination. There were approximately forty petals in the structure of the lesions.

4 In the posterior portion of the lens, another opacity was visible, which by reflected light seemed to have the appearance of a "bomber flying directly overhead, with most of the tail torn away." With the narrow beam of the slit lamp, the posterior portion of the lens could be seen to bulge backward in a characteristic manner through the space represented by the outline of the framework of the wing of the plane, the bulge producing a strangely unique traumatic lenticulus posterior. The aforementioned "framework of the wing" was seen to coil on itself and produce a reduplication line, the opacity calling to mind glass tubings.

The entire opacity in the posterior section of the lens was much more dense than that in the region of the "sunflower," and whenever a ray of light was so directed that it struck the posterior part of the lens, the anterior part of the "sunflower" was rendered invisible. This posterior opacity was thickest in the central (polar) region and when viewed in the zone of specular reflection had a polychromatic luster. The reduplication lines on the posterior capsule extended across the lens, from the nasal to the temporal side.

From the posterior polar region of the opacity a long, thin, brownish line extended into the inner lenticular structure to a region just back of the posterior Y suture.

The anterior portion of the vitreous showed many indications of degeneration. The fibrous network was dense, and the interfibrillar spaces were optically empty. The latter change was present for only a small distance posterior to the lens. The adjacent region was more dense than normal, and the vitreous had a milky appearance, with more than the normal amount of horizontal interlacing fibers. In this area there was some play of color, the horizontal small lines appearing reddish with a noticeable interspersing of blue. Intermixed with these fibers were several irregular,

vertically running, rootlike fibers, free of branching structures

Von der Heydt,<sup>2</sup> Jess<sup>3</sup> and Vogt<sup>4</sup> showed that the copper particles lie in the region of the epithelial cell layer, with deposition in the protoplasm and with the nucleus of the cell remaining free of the copper substance. Vogt's histologic studies showed that the deposition of copper is mainly in the epithelium of the lens. Jess expressed the belief that the radiate appearance of the "sunflower" is related to the direc-

tion and morphologic character of the radial folds of the iris, the copper particles being deposited in the so-called depressions of the radial structure of the iris.

Purtscher,<sup>5</sup> in 1918, pointed out that the "sunflower" is diagnostic of retained copper. Zur Nedden<sup>6</sup> described a case of chalcosis lentis in which the characteristic copper substance disappeared from the lens several years after removal of the intraocular foreign body. The onset of appearance of the characteristic changes of chalcosis depends on the amount of copper introduced, the location of the foreign body and the rate of decomposition of the metal.<sup>7</sup> The final color and morphologic features of the "sunflower" will depend on the amount of copper carbonate which is deposited.

2 von der Heydt, R. Ocular Chalcosis, *Am J Ophth* **18** 1045, 1935

3 Jess, A. Der histologische Bild der Kupfertrübung der Linse, *Klin Monatsbl f Augenh* **68** 432, 1922, Verkupferung der Zonulafasern und der teilweise abgelosten Zonulalamelle bei luxiertem Kupferstar, *ibid* **76** 465, 1926, Das Verschwinden der Verkupferungserscheinungen des Auges, *Centralbl f prakt Augenh* **53** 172, 1929

4 Vogt, A. Atlas of the Slitlamp-Microscopy of the Living Eye, translated by R. von der Heydt, Berlin, Julius Springer, 1921, vol 2, Chalcosis von Linse und Glaskörper, *Klin Monatsbl f Augenh* **67** 560, 1921

5 Purtscher. Kupfer in Glaskörper, *Zentralbl f Augenh* **42** 172, 1918

6 zur Nedden. Mitteilungen über ein eigenartiges Verhalten von Kupferstückchen im menschlichen Auge, *Klin Monatsbl f Augenh* **41** 484, 1903

7 Müller, H. K. Ueber die Verkupferung des Auges und ihre Behandlung, *Schweiz med Wchnschr* **67** 790, 1937

# Clinical Notes

## RECONSTRUCTION OF ABLATED LOWER LID

HAROLD F WHALMAN, M D

Clinical Professor of Ophthalmology, College of Medical Evangelists  
LOS ANGELES

The axiom "Necessity is the mother of invention" finds frequent fulfilment in the sphere of surgery, particularly, perhaps, in the field of reconstructive surgery where conditions are constantly at variance and ingenuity takes precedence over established procedures in meeting the requirement of each case. Hence the report of a newly devised procedure in no way disparages the value of previously reported methods, and if it solves a particular problem, it would seem odious to review, discuss and rationalize all other operations in order to justify the usefulness of one. The method I am about to describe arose out of the necessity for extensive ablation of the right lower lid in a case of basal

punctum. The tarsal plate and conjunctiva of the lid were then included in the excision, scissors being used to complete the ablation. The lower canaliculus was split for drainage.

The first step after ablation was to prepare a broad-pedicled cutaneous flap from the upper lid in the following manner. A curvilinear incision was made in the skin, in a natural crease about 5 mm distal to the upper margin of the lid, with inclusion of the orbicularis muscle. The skin was then carefully undermined just

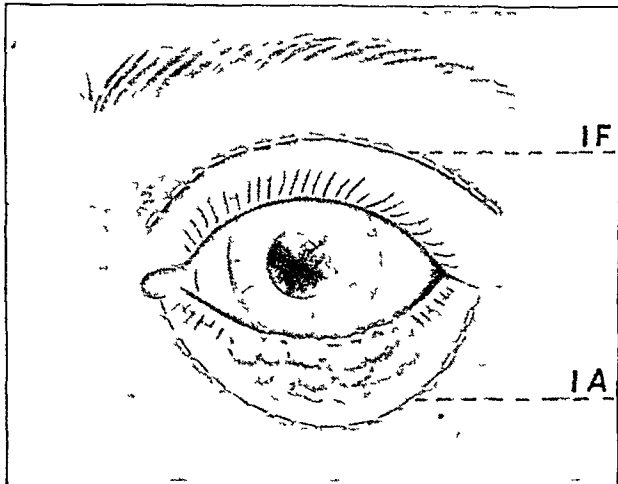


Fig 1—Formation of a cutaneous flap from the upper lid in the reconstruction of an ablated lower lid. IF indicates incision for flap, and IA, incision for ablation.

cell carcinoma which had grown in both directions laterally from the middle of the lower lid and had invaded the tarsal cartilage. The growth was invasive and did not subside with moderate irradiation, and since a larger dose would have resulted in destruction of the lid, excision, with a safe margin, seemed advisable.

The lower lid was therefore excised by sharp dissection, the incision beginning at the external canthus and taking a curvilinear course through the skin down along the inferior orbital margin to about 3 mm to the nasal side of the

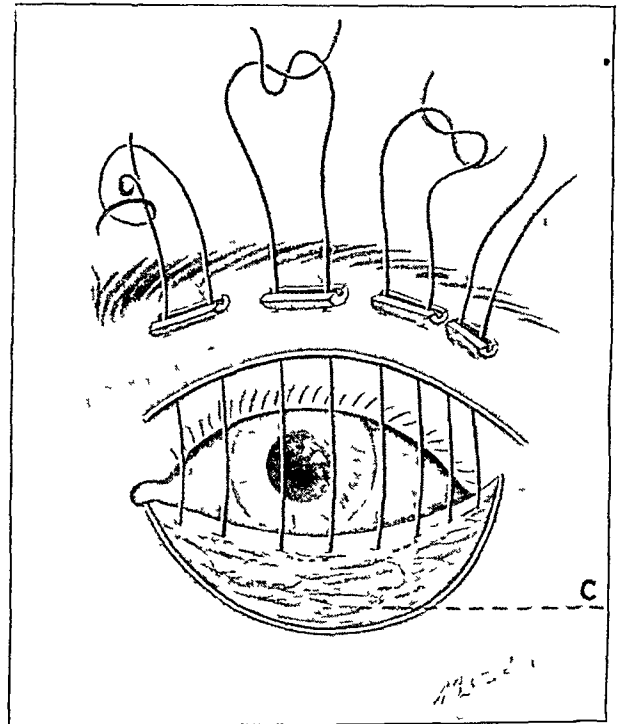


Fig 2—Placing of the sutures in the conjunctival flap (from lower lid) and the cutaneous flap from the upper lid. C indicates the conjunctiva undermined.

beneath the orbicularis muscle for a distance of 15 mm to make a skin-orbicularis muscle flap (fig 1).

In the second step of the operation the conjunctiva of the lower cul-de-sac was undermined down to the fornix. (There is considerable conjunctivitis in the fornix even after removal of the lid, furthermore, it can be stretched considerably after it is undermined.) Into the conjunctival flap four double-armed black silk sutures were inserted from the conjunctival side, and each, in turn, was then inserted through the orbicularis muscle-skin flap, coming out in

Presented as a preliminary report at the Forty-Eighth Annual Meeting of the American Academy of Ophthalmology and Otolaryngology, Section on Ophthalmology, Chicago, Oct 12, 1943.

the skin (fig 2) These sutures were tied over small pieces of rubber on the cutaneous side, so that the skin-orbicularis muscle flap had a conjunctival lining, of course, the eyeball was then obscured The free margin of the flap was then united to the skin-muscle edge of the incision made through the lower lid by means of closely placed interrupted black silk sutures (fig 3)

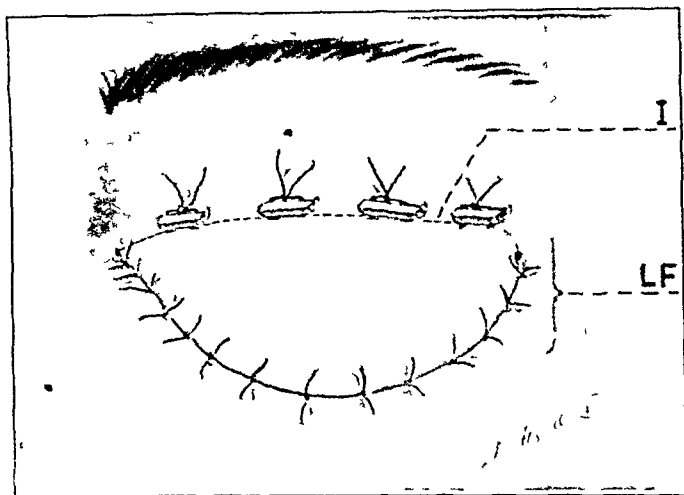


Fig 3—Cutaneous flap from the upper lid in place *I* indicates final incision to free graft, and *LF*, lid flap, lined with conjunctiva (eye obscured)

Union was allowed to take place for ten days, then all sutures were removed, and the flap from the upper lid was severed from its base The margins of the wound in the upper lid were trimmed and united, and the edges of the skin and conjunctiva of the new lower lid were sutured together with interrupted stitches, so that a cleanly united upper lid was left and a cutaneous flap replaced the ablated skin of the lower lid (fig 4)

The new lower lid was actually larger than needed, but the excess was not trimmed to allow for shrinkage

Two months later little shrinkage had taken place, so the lower lid was reduced to better size by excising some of it at its margin

The lower canaliculus, which had been split, remained patent, and because the lower lid of the fellow eye had imperceptible eyelashes, no attempt was made to implant hair-bearing skin for lashes It is my opinion that lashes on the

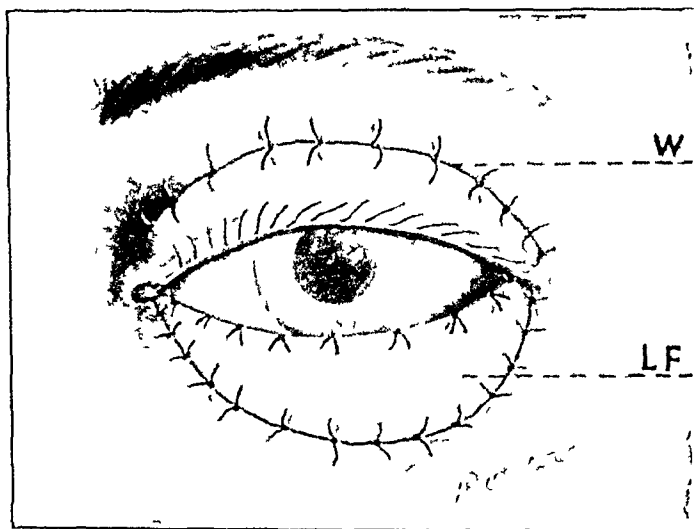


Fig 4—Final step in reconstruction of the ablated lower lid *W* indicates wound in upper lid united, and *LF*, lid flap excised from the base, ten days after union

lower lid are usually so inconspicuous that the procedure is not always necessary for good appearance

Exceedingly good function and appearance have resulted from the operation described The lid is fully reconstructed except for the cartilage, which does not seem to be important in the lower lid The finished work is smooth and even with no perceptible scars, as union takes place in natural folds of the upper, as well as the lower, lids

727 West Seventh Street

# UNSUCCESSFUL TREATMENT OF SYPHILITIC INTERSTITIAL KERATITIS WITH SULFANILAMIDE

ROY O SCHOLZ, M D  
BALTIMORE

Sandler<sup>1</sup> published a case in which congenital syphilitic interstitial keratitis failed to respond to antisyphilitic and foreign protein therapy but rapidly cleared after systemic treatment with azosulfamide (disodium 4-sulfamidophenyl-2'-azo-7'-acetylamino-1'-hydroxynaphthalene-3', 6'-disulfonate) and sulfanilamide. After this report Arena<sup>2</sup> reported 7 additional such cases in which the patients were treated orally with sulfonamide drugs. The clearing of symptoms was described as "remarkable." He stated that evidence as to the pathogenesis of interstitial keratitis does not substantiate the theoretic value of sulfonamide compounds but he felt that his empiric results justified the use of these drugs in conjunction with antisyphilitic therapy.

Four patients with congenital syphilitic interstitial keratitis were treated in the Johns Hopkins Hospital with ordinary antisyphilitic therapy plus sulfanilamide in larger doses than was used by Arena, and in none of these was there any significant improvement which might be attributed to this therapy. One of these patients was also given a second course of treatment with sulfanilamide plus riboflavin, without effect. In all 4 patients the usual chronic course of the disease followed,<sup>3</sup> inflammation gradually subsiding as corneal vascularization became complete.

## REPORT OF CASES

**CASE 1**—D S, a 9 year old white girl, was admitted ten days after the onset of interstitial keratitis. The serologic test for syphilis gave a positive result, and other stigmas of congenital syphilis were present. She received one injection of mapharsen and doses of sulfanilamide (1 Gm three times a day) for eleven days, an average level of 4 mg per hundred cubic centi-

From the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital.

Marv S Goodwin, M D, of the Syphilis Division of the Medical Clinics, cooperated in the study of these cases.

1 Sandler, I L. Sulfanilamide Treatment of Syphilitic Keratitis. Preliminary Report, *Arch Dermat & Syph* 39 528 (March) 1939.

2 Arena, J M. Use of Sulfonamides in Treatment of Syphilitic Keratitis, *J Pediat* 20 421 (April) 1942.

3 Woods, A C. Syphilis of the Eye, *Am J Syph, Gonorr & Ven Dis* 27 133 (March) 1943.

eters of blood being maintained. The keratitis at first consisted of central, deep infiltration, but during the course of this therapy the infiltration gradually increased in size and the cornea became heavily vascularized.

After the patient's discharge antisyphilitic therapy was continued, and two months later she was readmitted because of extreme photophobia and lacrimation. During this hospitalization she was given the same dose of sulfanilamide as before (1 Gm three times daily) and riboflavin (5 mg twice daily) for nine days. The keratitis did not improve. One month after her second discharge the inflammation began to subside, and it completely disappeared approximately seven months after the onset.

**CASE 2**—L M S, a 21 year old Negro woman, was found to have a positive serologic reaction for syphilis in a routine examination. She had had poor vision since the age of 11 but had had no active symptoms until one month before admission, when her left eye became sore. Six months prior to admission she had had a generalized cutaneous eruption. Her condition was diagnosed as congenital syphilis and syphilitic keratitis of the left eye.

She had received injections of mapharsen and was receiving her first doses of bismuth when she was admitted for systemic treatment with sulfanilamide. The right eye was essentially normal, and the left eye showed the typical picture of syphilitic interstitial keratitis. The vessels extended about 4 mm from the limbus, and there was a mild complicating anterior uveitis. She was given 3 Gm of sulfanilamide on admission and 1 Gm every four hours thereafter, a level of 75 mg per hundred cubic centimeters of blood being reached. During the eleven days of this treatment the vessels regressed slightly and the eye became somewhat clearer. She was discharged, showed slight improvement for three months and then had a recurrence in the right eye, which remained abnormal for an additional six months.

**CASE 3**—F M J, a white youth of 16, was admitted because of a positive serologic reaction for syphilis and interstitial keratitis. The patient's mother also gave a positive reaction to a serologic test for syphilis. At the age of 10 he had had a penile lesion. His left eye was sore for six weeks prior to admission. His right eye showed marked lacrimation, blepharospasm and conjunctival injection but no corneal lesion. The left eye showed a typical picture of interstitial keratitis with photophobia, lacrimation and blepharospasm. The cornea was gray and fairly opaque, with small vessels progressing from the limbus almost to the center. He was given sulfanilamide, 1 Gm every four hours for eight days, a level of 5 mg per hundred cubic centimeters of blood being maintained. No great difference was noted either in the clearness of the cornea or in

the reduction of the infiltrating vessels when the patient was discharged or when seen three weeks later

CASE 4—M H, a Negro girl aged 11 years, had had her first attack of interstitial keratitis at the age of 5. Both of her parents gave a history of having received antisyphilitic treatment. She responded well at that time to syphilitic therapy and continued to take routine treatments with bismuth and arsphenamine. Eight weeks before admission she began to have difficulty with walking, and for six weeks before admission she had increasing deafness and complained of tinnitus. Four weeks before admission the left eye had a recurrence of interstitial keratitis.

The child was completely deaf, and examination was difficult. The right eye presented the picture of old healed interstitial keratitis. The left eye showed extreme photophobia and lacrimation. There were a number of infiltrations scattered over the cornea and numerous layers of deep dilated vessels, which covered the whole cornea. She was given 1 Gm of sulfanilamide every four hours, a level of 14 mg per hundred

cubic centimeters of blood being maintained. During her three weeks' hospitalization the photophobia and lacrimation almost completely disappeared, and the congestion subsided. The vascular picture and the infiltrations remained the same. Vision could not be tested because of the complete deafness of the child. She was seen in the dispensary one month later, when further improvement was noted. This is the only patient in whom a suggestion of improvement was found, and that improvement took place only after the vessels had coalesced.

#### SUMMARY AND CONCLUSIONS

The addition of large doses of sulfanilamide to the usual antisyphilitic therapy in the treatment of 4 patients with congenital syphilitic interstitial keratitis did not prove of any benefit. Healing of the cornea took place, as usual, only after vascularization was complete. I do not believe sulfanilamide therapy is indicated in the treatment of this disease.

# Ophthalmologic Reviews

EDITED BY DR FRANCIS HEED ADLER

## MODERN TRENDS IN OCULAR THERAPEUTICS

ROY O RISER, M D

PARK RIDGE, ILL

This summary of certain trends in ocular therapeutics was made at the request of the Committee on Scientific Exhibits of the American Academy of Ophthalmology and Otolaryngology. The material has been taken from rather recent literature and is not a complete review. Complete bibliographies will be found in some of the latest articles.

### THE EYELIDS

Lesions of the dermal surface of the eyelids and of the lid margins may be associated with infections of the conjunctiva or may result from the use of medicaments, such as physostigmine or atropine, for deeper diseases of the eye. Dermatologic diseases or systemic disturbances may also affect the lids.

Some lesions of the lids are best treated by specific medication directed at the bacterial cause, such as the use of sulfathiazole ointment and staphylococcus toxoid for staphylococcal blepharitis. Vitamin therapy or regulation of diet is of aid in the therapy of other conditions. Allergic reactions involving the lids and angioneurotic edema may require special tests and still other forms of treatment.

The seborrhea of puberty requires different treatment than does stagnation of the sebaceous glands of senility. The relative value of oily medicaments, such as cod liver oil, and of fat-dissolving solutions, such as purified benzene (to be used with caution), for cleansing dry and crusted lids must also be given careful consideration, as stressed by Links<sup>1</sup>. He emphasized the necessity of cleansing the lids but warned that soap, water and hot packs may perpetuate certain conditions.

Many disturbances of the lids are easily made worse by overmedication. The best therapy is often the simplest and mildest dermatologic preparation that makes the patient comfortable while the cause is being investigated and eliminated. Links described the pharmacologic action of the following types of such preparations:

<sup>1</sup> Links, A. Applied Pharmacology of the Skin in the Ophthalmologist's Everyday Practice, Arch Ophth 28 959 (Dec) 1942

**Powders**—Powders such as talc and zinc oxide may be chiefly protective, or magnesium carbonate may be used for its adsorbing and mild antiphlogistic effect. Oozing or weeping surfaces must not be treated with powders.

**Lotions**—Powder in water, with or without glycerin, is also used for dry lesions.

**Calamine Lotion N F** This preparation constitutes the standard treatment for simple dermatitis.

**Disinfectant Lotion (Lutz)** Use of such a lotion is advisable in treatment of eczematous impetigo.

	Gm or Cc
Resorcinol	0.2
Ichthammol	0.5
Zinc oxide	
Talc	āā 15
Dilute alcohol	
Distilled water	āā ad 100

The danger of resorcinol dermatitis should be borne in mind.

**Cold Cream**—"Cold" cream, or "refrigerating cream" (rose water ointment U S P), is especially good for dry skin. The essential oils in cold cream may be irritating.

A substitute for cold cream, to be used for irritated lids, may be made up as follows:

	Gm or Cc
Wool fat	
Boric acid, 2 per cent solution	āā 10
White petrolatum	5

An astringent and mild disinfectant (Seibert) may be desired:

	Gm or Cc
Solution of aluminum acetate	2
Distilled water	5
Wool fat	
White petrolatum	āā 10

**Pastes**—Pastes are mixtures of powder and grease and are useful in treatment of broken or weeping surfaces or of surfaces macerated by persistent epiphora. The following preparations are mentioned:

**Lassar's Zinc Oil** (for maceration and for fissures)

Zinc oxide	6 Gm
Olive oil	4 Gm

Ichthammol (0.5 Gm) may be added to increase the antiseptic properties

Lassar's Zinc Paste (for dermatitis, such as that due to atropine or hair dye)

Zinc oxide  
Talc  
Wool fat  
White petrolatum   āā 10 Gm

Atkinson's Paste (for eczema or herpes zoster of the lids)

Bismuth subnitrate                   2.5 Gm  
Wool fat  
Zinc oxide ointment U S P   āā 15.5 Gm

*"Refrigerating Pastes"*—These preparations can be applied to most irritated skins. Links<sup>2</sup> stated that if he is in doubt as to the diagnosis of a lesion of the lids or as to the best treatment he usually resorts to a refrigerating paste which can do little harm. Links<sup>2</sup> mentioned the following preparations:

Neisser's Paste (for chronic inflammation of the lid margins)

Zinc oxide  
Bismuth subnitrate           āā 0.5 Gm  
Rose water ointment  
Cerate U S P           āā 10.0 Gm

Substitute for Neisser's Paste (for patients sensitive to oils in rose water ointment U S P)

Gm or Cc  
Magnesium carbonate           5  
2 per cent solution of boric acid  
White petrolatum           āā 10

Stein's Paste (for fissures of lid margins)

Gm  
Ichthammol                   0.1  
Zinc oxide  
Bismuth subnitrate           āā 1.0  
Rose water ointment U S P   10.0

Slight oozing or weeping is not a contraindication.

*Ointments*—An ointment consists of an active drug in a viscous base. A variety of bases, used alone or in combination, are available.

1 Petrolatum as a base is used chiefly for chronic lesions when deeper penetration of the active drug is desired. Water-soluble drugs cannot be applied in petrolatum, but it may serve as a base for other drugs. Peter's ichthyol zinc ointment, for the treatment of rosacea of the lids is such a preparation.

Gm  
Ichthammol                   0.15  
Zinc oxide                   0.50  
White petrolatum           15.00

2 Wool fat is usually combined with petrolatum because it forms an emulsion with water

and watery solutions of active drugs. Such a preparation is bismuth tetralnomopyrocatechin (noviform), used for chronic blepharitis in 10 per cent concentration in an ophthalmic ointment base made of wool fat, water and petrolatum.

3 A base made of cholesterol derivatives and petrolatum is also miscible with drugs in aqueous solutions. This has been used for seborrhea of the lid borders by Gifford.<sup>3</sup>

Gm  
Naphthalan                   2.0  
Ichthammol                   0.6  
Zinc oxide  
Starch                   āā 8.0  
Oxysterol-petrolatum  
base                   qs 30.0

4 Wetting Agents. Commercial detergents of low surface tension although still in the semi-experimental stage for ophthalmic medication will undoubtedly be the next addition to ophthalmic ointment bases. For further details the reader is referred to the last paragraph of the section on "Better Eye Drops."

#### GLAUCOMA

The following therapeutic agents are available:

*Acute Glaucoma*—1 Physostigmine salicylate (or sulfate), in 0.5 to 2 per cent solution. Five drops is instilled at one minute intervals, and the instillations may be repeated in one hour and, again, in three hours, as indicated. The solution may be combined with a 2 per cent solution of pilocarpine nitrate, if desired.

2 Morphine sulfate, given by hypodermic injection, for pain. Administration may aid in induction of miosis.

3 Magnesium sulfate, as a purgative, for reduction of fluids.

4 Hypertonic solutions given intravenously, for reduction of fluids.

(a) Sodium chloride. Fifty cubic centimeters of a 30 per cent solution (or 150 cc of a 10 per cent solution). It acts the most rapidly of the three solutions indicated, being effective in less than five to eight hours.

(b) Dextrose. One hundred cubic centimeters of a 50 per cent solution. The effect is slower and more prolonged than that of the hypertonic solution of sodium chloride.

2 The ointment base is made by the Manhattan Eye Salve Company.

3 Gifford, S. R. *Hand-Book of Ocular Therapeutics*, ed. 3, Philadelphia, Lea & Febiger, 1942, chap. 6.

4 Manufactured by Abbott Laboratories, North Chicago, Ill.



(c) Sorbitol One hundred cubic centimeters of a 50 per cent solution The effect is greatest twelve to twenty-four hours after injection

5 Glycerin Corneal edema may be cleared in thirty seconds by instillation of drops of full strength glycerin The clearing lasts for several minutes and, according to Cogan,<sup>5</sup> does no harm

6 Alternatives for physostigmine Other miotics for treatment of acute glaucoma are

(a) Neostigmine bromide, in 5 per cent solution, usually used with a 20 per cent solution of mecholyl chloride Repeated instillations may be made, with or without retrobulbar injection of 10 to 20 mg of mecholyl chloride This injection may have dangerous effects, the antidote is atropine The aforementioned combination is more advisable for use in the early stages of acute glaucoma

(b) Furfuryltrimethylammonium iodide (furmethide), in 10 per cent solution One drop is instilled every fifteen minutes for two hours, and then every three hours until tension becomes normal or operation is performed This drug is more advisable for use in the later stages of acute glaucoma

(c) Histamine This substance is the most powerful miotic available, but is not advisable for use because of the severe reaction it induces

7 Surgical intervention Operation must not be delayed if tension remains at an unsatisfactory level for more than a few hours

*Chronic Glaucoma*—The following substances are available for therapy

1 Pilocarpine nitrate, in a 1 to 2 per cent solution two or six times daily

2 Physostigmine salicylate (or sulfate), in 0.25 to 0.5 per cent solution, alone or to increase the action of pilocarpine This substance often causes sensitivity when used over long periods of treatment in chronic glaucoma

3 Neostigmine bromide, in 3 per cent solution This substance may be used alone, as a substitute for pilocarpine, but is usually combined with mecholyl chloride, 10 per cent, to give a synergistic effect Mecholyl is not used alone

4 Carbaminoylcholine chloride, in 0.75 to 1.5 per cent solution It is much more effective in a 1:3,000 solution of zephiran chloride, giving results equal to those with a 2 per cent solution of pilocarpine nitrate or a mixture of 2 per cent pilocarpine nitrate and 0.5 per cent physostigmine

salicylate (or sulfate) Clarke<sup>6</sup> claimed that other miotics are more effective after a period of rest induced with carbaminoylcholine

5 Furfuryltrimethylammonium iodide, in 10 per cent solution This substance is slightly more effective than a 2 per cent solution of pilocarpine nitrate for chronic glaucoma but, like the other new miotics, does not replace it<sup>7</sup> It is an adjuvant in the medical treatment, for if one miotic is no longer tolerated another may still keep the tension lowered

6 Epinephrine and its derivatives These substances, while causing mydriasis, lower the intraocular tension Miotics are to be used before and after administration of these drugs, which is not advisable in treatment of glaucoma other than the simple chronic type

(a) Epinephrine hydrochloride Four minims (0.25 cc) of a 1:1,000 solution is injected subconjunctivally, or 5 minims (0.31 cc) of a 1:1,000 solution on a cotton pledget is inserted in the upper cul-de-sac for four minutes (Gradle's method)

(b) Synthetic dextrorotary epinephrine 2 per cent solution

(c) Epinephrine bitartrate in 2 per cent solution (J Green)

(d) Neo-synephrine hydrochloride either in 10 per cent emulsion or in 10 per cent solution in the new low surface tension vehicle (Frederick Stearns & Company)

The treatment of glaucoma is discussed by Gifford<sup>8</sup> in greater detail

NOTE OR CAUTION—The action of these agents is increased by promotion of the general health, elimination of other disease when possible and abstinence from tobacco, coffee and table salt The visual fields should be watched, and tonometric records should be kept Surgical treatment may be indicated

#### INDICATIONS FOR SULFONAMIDE COMPOUNDS IN OPHTHALMIC PRACTICE

*Oral Administration*—To obtain standard concentrations in the blood of 5 to 10 mg per hundred cubic centimeters, administration of at least 0.5 Gm (7.7 grains) every two hours for adults is advised If several sulfonamide compounds have been employed or recommended for

6 Clarke, S T Use of Doryl in Treatment of Glaucoma, *Am J Ophth* 25 309 (March) 1942, Mecholyl and Prostigmine in Treatment of Glaucoma, *ibid* 22 249 (March) 1939

7 Uhler, E M Use of Furmethide in Comparison with Other Miotics for Treatment of Glaucoma, *Am J Ophth* 26 710 (July) 1943

8 Gifford,<sup>8</sup> chap 11

5 Cogan, D G Clearing of Edematous Corneas by Glycerine, *Am J Ophth* 26 551 (May) 1943

a certain disease, with apparently equally good results, sulfadiazine is indicated because it is least toxic. Foreign protein, when indicated, may be given with full doses of the chosen sulfonamide compound.

*Local Use*—The substances are given as powders, solutions, emulsions and ointments and by iontophoresis, and now incorporation of the less permeable sulfonamide compounds in "wetting agents," which Bellows<sup>9</sup> has tried experimentally, promises even greater local use of medicaments at present given internally, with due consideration of possible toxicity. Insufflation of powders every three to four hours is useful if the patient is hospitalized.

A discussion of the chemotherapy of infections of the eye by Thygeson<sup>10</sup> is summarized in the following tabulation.

Disease	Organism	Oral or Local Use	Sulfonamide Compound Indicated
Trachoma	Virus	Oral	Sulfanilamide still advisable
Inclusion conjunctivitis	Virus	Local (oral as indicated)	Sulfathiazole
Lymphogranuloma venereum	Virus	Oral	Sulfadiazine
Gonorrheal ophthalmia	Gonococcus	Oral (powder applied locally is optional)	Sulfadiazine
Erysipelas (lids)	Streptococcus B haemolyticus	Oral	Sulfanilamide still advisable
Impetigo		Local	
Dacryocystitis (acute)		Oral	
Conjunctivitis		Local	
Corneal ulcer		Both	
Panophthalmitis	Staphylococcus	Oral	Sulfathiazole
Blepharitis		Local (and staphylococcus toxoid)	
Conjunctivitis		Local	
Marginal corneal ulcers		Local (powder)	
Impetigo		Local	
Recurrent hordeolum	Pneumococcus	Local	Sulfathiazole
Corneal ulcer		Both (powder)	
Conjunctivitis		Local	
Corneal ulcer		Both (powder or by iontophoresis)	
Conjunctivitis	Bacillus Friedlander or Bacillus pyocyaneus	Local (other medications are not to be discarded)	Sulfathiazole
Penetrating injury			
Sympathetic ophthalmia	Several ?	Oral (local, optional)	Sulfadiazine
		Oral	Sulfanilamide (Not a cure)
Endophthalmitis	Meningococcus and others	Oral (and by iontophoresis [?]) (penicillin probably of more avail for such metastatic lesions)	Sulfanilamide Sulfadiazine?
Uveitis	Several	Oral, if at all	Sulfadiazine(?)

A number of reports, personal experiences, and the like, indicate that the sulfonamide compounds are disappointing in treatment of uveitis.

<sup>9</sup> Bellows, J. Chemotherapy in Ophthalmology, Tr Am Acad Ophth 47:19 (Sept-Oct) 1942, Arch Ophth 29 888 (June) 1943.

<sup>10</sup> Thygeson, P. Sulfonamide Compounds in Treatment of Ocular Infections, Arch Ophth 29 1000 (June) 1943.

They may be tried with foreign protein therapy; administration of salicylates, specific therapy, such as use of tuberculin or antisyphilitic drugs, and removal of foci of infection.

#### BETTER EYE DROPS

The following factors are to be considered in the evaluation of eye drops.<sup>11</sup>

1 *Tonicity*—Solutions isotonic with tears are generally least irritating. Tears are isotonic with a 1.4 per cent solution of sodium chloride.

2 *Hydrogen Ion Concentration*—The acidity or the alkalinity is a common, and more important, cause of irritation from eye drops. This is measured in terms of the  $p_H$ , which indicates the hydrogen ion concentration. The  $p_H$  also influences the solubility and activity of the drug. Pure water has a  $p_H$  of 7, acids have a  $p_H$  of

less than 7, and alkalis, a  $p_H$  of more than 7. The more nearly the  $p_H$  of the eye drops approaches the average  $p_H$  of tears (7.5), the more com-

<sup>11</sup> Various problems associated with ophthalmic solutions have been discussed by the following authors: Elvin, N. C. The  $p_H$  and Tonicity of Ophthalmic Solutions, Arch Ophth 29 273 (Feb) 1943. Gifford,<sup>a</sup> chap 3. Gifford, S. R., Puntney, I., and Bellows,

fortable they are, but the drugs vary with respect to such factors as chemical composition, solubility and optimum rate of absorption

**3 Buffer Solutions**—Such solutions resist changes in  $p_H$  by diluents, such as the lacrimal secretions. An almost constant  $p_H$  can be maintained by the correct selection of the type and proportion of acid or alkaline constituents. Buffered eye drops are less irritating, and the drugs they contain are more readily absorbed.

The recommended hydrogen ion concentrations, in terms of the  $p_H$  of various forms of buffered eye drops, is tabulated as follows

#### Ophthalmic Solution

$p_H$	
50	Butacine sulfate, phenacaine hydrochloride (the solution must be warmed)
59	Eucatropine hydrochloride, in a special buffer formula
60	Zinc, cocaine, epinephrine, paredrine hydrobromide ophthalmic and 2 per cent boric acid
67	Tetracaine hydrochloride in isotonic solution of sodium chloride (do not buffer)
675	Special buffered, isotonic, preserved solution of zinc sulfate, recommended by Arrigoni and associates <sup>12</sup>
76	Homatropine, atropine, scopolamine, physostigmine, pilocarpine. Buffer solution for use alone, as a general collyrium
84	A buffer solution alone, for the secretions of vernal catarrh
86 }	Buffered solutions for wearers of contact
88 }	lenses <sup>13</sup>
90	Vehicle for fluorescein, requiring alkaline solution (fluorescein sodium is soluble in pure water)

**Easy Method of Prescribing for Buffer Solutions** With the buffer solutions recommended by Gifford and Smith<sup>14</sup> and Feldman,<sup>15</sup> mixtures of two stock solutions are used in varying proportions to obtain the required  $p_H$ . To 30 cc of the acid stock solution a standard fixed amount, is added a smaller amount of alkaline

stock solution to produce the  $p_H$  desired. One may specify Gifford's buffer solution or Feldman's buffer solution to the druggist in the manner shown in the following prescriptions, for practically all the pharmacies of the country receive the "Blue Book,"<sup>16</sup> which contains the exact information they need to fill such prescriptions

R	Atropine sulfate	0.15 Gm
	Gifford's buffer solution, $p_H$ 7.6	15 cc
R	Zinc sulfate	0.02 Gm
	Feldman's buffer solution $p_H$ 6.0	15 cc

**4 Preservatives** (for prevention of yeast or fungus growths) —The following substances are suggested

Boric acid, 40 grains (2.6 Gm) to the ounce (31 Gm) or in the proportion used in buffer solutions

Chlorobutanol, 0.5 or 1 per cent. This substance will not change the  $p_H$  of buffer solutions

Camphor or menthol, 1 grain (0.065 Gm) to the ounce

Benzoic acid esters are ideal preservatives but are not universally obtainable. The propyl and methyl esters<sup>17</sup> may be used in stock buffer solutions. They are especially good for preventing molds in damp climates

**5 Substitutes for Tears**—Buffer solution  $p_H$  7.6 may be used as a collyrium. Use of gelatin in Locke's solution was advised by Rucker for deficiencies in secretion of the lacrimal gland (keratoconjunctivitis sicca)

Gelatin 0.3 Gm, chlorobutanol, 0.15 Gm, Locke's solution 30.0 cc

Locke's solution consists of sodium chloride, 0.9 Gm, potassium chloride, 0.024 Gm, calcium chloride, 0.042 Gm, dextrose, 0.1 Gm, sodium carbonate, 0.02 Gm and distilled water, 100 cc

**6 Surface Tension**—The surface tension of medicated eye drops (and of ophthalmic ointments) assumes increasing importance in the light of recent reports

**Emulsions of Oil in Water** These have been tried, especially for mydriatics and cycloplegics but have not yet found general favor

**Aqueous Vehicles of Low Surface Tension** These preparations are more practical. One developed for neo-synephrine ophthalmic solution (see section 6 *d* under "chronic glaucoma") is now offered as a general ophthalmic

J. G. Keratoconjunctivitis Sicca, Arch Ophth 30 207 (Aug) 1943. Hosford, G. N., and Hicks, A. M. Hydrogen Ion Concentration of Tears: Its Relation to Certain Ocular Symptoms and to Conjunctival and Corneal Lesions, ibid 13 14 (Jan) 1935. Swan, K. C., and White, N. G. Corneal Permeability Factors Affecting Penetration of Drugs in Cornea, Am J Ophth 25 1043 (Sept) 1942

12 Arrigoni, L., Fischer, L., and Tozer, G. A. Ophthalmic Zinc Sulfate Solutions: Buffered, Isotonic and Preserved, Arch Ophth 26 852 (Nov) 1941

13 Obrig, T. Contact Lenses, New York, Obrig Laboratories, Inc., 1942, chap 9

14 Gifford, S. R., and Smith, R. D. (a) Effect of Reaction on Ophthalmic Solutions, Arch Ophth 9 227 (Feb) 1933. (b) Gifford S. R. Reaction of Buffer Solutions and of Ophthalmic Drugs, ibid 13 78 (Jan) 1935

15 Feldman, J. B.  $p_H$  and Buffers in Relation to Ophthalmology, Arch Ophth 17 797 (May) 1937

16 American Druggist Blue Price Book, revision 15, 1943, blue section, pp 31 and 32

17 Available as nipagin M and nipasol M, respectively, from the Goldschmidt Corporation, New York

vehicle<sup>18</sup> It contains a detergent, or "wetting agent, benzoic acid esters as preservatives and an isotonic solution of sodium chloride It is compatible with fourteen common ophthalmic drugs

"Wetting Agents" These represent the latest trend toward more efficient ophthalmic drops and ointments Substances which lower interfacial tension between the corneal epithelium and the surrounding media produce an increased penetration of the cornea by the medicament in the wetting agent A new field for medication of the anterior segment, especially for drugs not easily absorbed by the cornea, has been shown by

---

<sup>18</sup> Obtainable from Frederick Stearns & Company, Detroit

O'Brien and Swan<sup>19</sup> in their use of zephiran chloride (a wetting agent) in augmenting the action of carbamoyl choline chloride and by Bellows and Gutmann<sup>20</sup> in their use of the sulfonamide compounds with commercial wetting agents such as the aerosols, the tergitols and the duponols

120 Main Street

---

<sup>19</sup> O'Brien, C S, and Swan, K D Carbamoyl-choline Chloride in Treatment of Glaucoma Simplex, Arch Ophth **27** 253 (Feb) 1942

<sup>20</sup> Bellows, J G, and Gutmann, M Application of Wetting Agents in Ophthalmology, with Particular Reference to Sulfonamide Compounds, Arch Ophth **30** 352 (Sept) 1943

# Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

## Cornea and Sclera

SOLAR KERATOCONJUNCTIVITIS ASSOCIATED WITH AMBLYOPIA C BERENS and P T McALPINE, *Am J Ophth* 27: 227 (March) 1944

Berens and McAlpine give the following summary

"1 Two brothers were exposed to an open carbon-arc lamp for three 15-minute periods within 48 hours 2 Following this, vision was reduced to the perception of hand movements and the visual fields to a temporal crescent in each eye 3 There was gradual recovery in the course of 11 days, both of visual acuity and visual fields 4 Consideration of effects of ultra-violet radiation make it probable that the contraction of the visual fields and temporary amblyopia in these patients were caused by the thermal effect of the carbon-arc lamp"

W S REESE

## Experimental Pathology

EXPERIMENTAL CORNEAL ULCERS J M ROBSON, *Brit J Ophth* 28: 15 (Jan) 1944

In the course of the work on experimental ulcer and infections of the cornea of various types, particularly experimental mustard gas lesions, it was found that secondary infection played an important part in determining the severity of the lesions produced by the mustard gas (dichloroethyl sulfide) Local treatment of rabbits with chemotherapeutic agents decreased the severity of the primary reaction and the liability to the development of delayed "vascularized keratitis" These experiments suggested that chemotherapeutic agents might be of value also in the treatment of lesions of the human eye due to mustard gas, and the treatment with sodium sulfacetimide is to some extent based on this work

In the human subject, many organisms may be concerned in the production of ulcer of the cornea With few exceptions, however, these various organisms do not produce a characteristic clinical picture The hypopyon type is usually due to the pneumococcus, but to some extent the etiologic agent varies with the geographic location and with the occupation of the patient Thus, in France for example, the diplobacillus of Morax (*Haemophilus duplex*) and that of Petit are not infrequently concerned In Palestine the Koch-Weeks bacillus (*Haemophilus influenzae*) was recovered In the Glasgow district *Staphylococcus aureus* was recovered in 25 per cent of the ulcers examined

The author describes the technic used in the experimental investigations on animals

*Pyocyaneus Ulcer*—Joy showed that the lesions were favorably influenced by the oral administration of sodium sulfapyridine The local application of a sulfonamide compound also had a favorable effect on the course of such lesions When a 30 per cent solution of sodium sulfacetimide was applied within one hour of inoculation, ulceration was completely prevented in more than half the treated eyes When administered after a delay of twelve hours, its value was greatly reduced, though there was still a definite effect

*Pneumococcus Ulcer*—The best results were obtained with penicillin, though striking effects were also seen with sodium sulfacetimide When treatment with penicillin was started within one hour after inoculation, ulceration was completely prevented in 7 of 8 eyes

*Lesions Due to Staph Aureus*—The local application of penicillin produced striking results Sodium sulfacetimide, though less effective, had a definite effect

*Lesions Due to Streptococcus Haemolyticus*—When treatment with penicillin (220 units per cubic centimeter) was started one hour after inoculation, the development of the lesion was almost completely inhibited

The investigation of the treatment of tuberculous lesions is still in an early stage

W ZENTMAYER

## Instruments

A REPORT ON DEFECTS FOUND IN TONOMETERS EXAMINED AT THE CHECKING STATION OF THE NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS M J SCHOENBERG AND A POSNER, *Am J Ophth* 27: 368 (April) 1944

Schoenberg and Posner reach the following conclusions

"A large percentage of tonometers (Schiotz type) contains defects of construction and of performance These defects point to one of the two reasons for the unreliability of many tonometers (the other reason is defective technique)

"Every tonometer already in use should be checked at a reliable checking station at the earliest possible time

"Inaccurate tonometers should not be used until the important defects are corrected or adjusted

"It is urgent that a number of reliable checking stations be established under the direction of ophthalmologists in appropriate locations, throughout this country

"It is important that precision mechanics be found who are able to put defective tonometers in good working order"

"Manufacturers of tonometers should be urged to have their instruments checked and certified at reliable checking stations before placing them on the market"

W S REESE

### Lens

THE DEVELOPMENT OF A SYSTEM OF INTRACAPSULAR CATARACT EXTRACTION D B KIRBY, *Am J Ophth* 27:124 (Feb) 1944

Kirby describes the development of a system of intracapsular cataract operations based on the condition of the capsule, cortex and zonule of the lens and the vitreous. In cases in which the zonule is resistant, after he has tried other procedures within the limits of safety, he strips off the zonule, according to a method he has devised

W. S REESE

CHOLESTERINOSIS LENTIS P GEORGARIOU and O WOLFE, *Am J Ophth* 27:394 (April) 1944

Georgariou and Wolfe give the following summary

"Pathogenic explanation of cholesterinosis lentis is based upon the pathogenic theory of lipoidosis bulbi. Conditions found outside the crystalline lens produce an infiltration of the posterior cortex of the crystalline-lens capsule. This infiltration follows a secondary disturbance of the lipid complex of the crystalline masses, producing the appearance of shining crystal of cholesterol"

"Cholesterinosis lentis is always a secondary cataract, and we should persist in detailed examinations to discover the primary causative factor"

W S REESE

### Neurology

INJURY TO THE OPTICO-CHIASMAL JUNCTION A CASE REPORT E B C HUGHES, *Brit J Ophth* 27:367 (Aug) 1943

The author reports a case of injury to the head from a head on motor crash. A man aged 31 sustained a fissured fracture running down in the left frontal bone, traversing the left frontal sinus and passing along the floor of the left anterior fossa lateral to the optic canal and then down into the left middle fossa. The actual course of this fracture was verified in the course of two operative procedures, one for an epidural hematoma on the left side, which was removed through a craniotomy opening in the temporal region, and the second, undertaken sixteen weeks after the injury for drainage of the aerocele cavity and repair of the dural defect over the frontal sinus. After the first operation vision in the left eye was limited to ability to count fingers in the upper nasal quadrant. Ten weeks after the first operation the left eye showed a large island of vision in the upper nasal quadrant

with macular vision of 1/60. Sixteen weeks after the injury the visual field of the right eye showed a large defect in the upper temporal quadrant and decrease of acuity in the lower temporal quadrant. After the second operation vision in the left eye improved to 6/36, as a result of enlargement of the island of vision to include the greater part of the macular vision. The field of the right eye lost its quadrantic defect but had a moderate-sized scotoma in the upper temporal portion. The site of the damage must have been either in the termination of the left nerve or in the anterior chiasmal angle—a lesion which corresponds to the "junction" type of defect. Such a lesion affects chiefly the fibers of the left optic nerve but also catches the knee of the crossed fibers from the lower nasal portion of the retina of the right eye. This case, while it fails to bring positive proof of the presence of this knee of fibers, nevertheless adds a little to the great weight of circumstantial evidence suggesting their presence. The fields are illustrated

W ZENTMAYER

OCULAR MANIFESTATIONS OF NEUROSIS COMMONLY FOUND AMONG SOLDIERS I C MICHAELSON, *Brit M J* 2:538 (Oct 30) 1943

Many soldiers, on account of fear and environmental stress, acquire a neurosis, of which there are two main varieties, hysteria and chronic anxiety state, the form being determined by the individual personality type. These conditions may cause symptoms referable to the eyes, in fact, half the soldiers in the outpatients' room of the ophthalmic department of a military hospital in the Middle East presented functional complaints, consisting of defective day vision, defective night vision, asthenopia, headache, photophobia, spots before the eyes and epiphora. These conditions are then more fully described, with the diagnosis and treatment. Functional diplopia and defective day or night vision are referred to as hysterias, while asthenopia, headache, photophobia and spots before the eyes are defined as a chronic anxiety state with ocular manifestations. The necessity of the exclusion of organic disease in cases of such a condition is self evident

The author concludes as follows: "It may be of some help to think of organic and functional disturbances coexisting in one of three different ways: (1) The association in one patient may be fortuitous. (2) A functional disturbance may be superimposed upon an organic one, modifying or aggravating the symptoms. (3) The psychic disturbance leading to upset of ocular function may appear to be an integral part of the organic process. This is noticed in disseminated sclerosis. It is not unusual in this disease for the 'functional' symptom to be the predominant one and to be present for a long period before the 'organic' symptoms arise."

This article is important and well worth careful study

ARNOLD KNAPP

### Ocular Muscles

OPHTHALMIC PRISMS, SOME USES IN OPHTHALMOLOGY G P GUIBOR, *Am J Ophth* 26: 833 (Aug) 1943

Guibor gives the following summary

"The action of prisms when placed before the eyes can be explained by the known physiologic phenomena of projection, reciprocal innervation, and synkinesis

"Prisms are of value in the diagnosis and treatment of motor disturbances produced by anisometropia and neuromuscular defects. The types of prisms most commonly used are the round, the square, the prism rack, the rotary, and the toric

"The nonsurgical treatment by prisms of divergence paralysis, concomitant convergent strabismus, and abducens paralysis is discussed, with figures to explain how prisms are applied therapeutically

"It must be understood that prisms are prescribed only after a therapeutic test is employed with the fivers. They should be prescribed on a neurologic and physiologic basis and not on mechanistic theory alone"

W ZENTMAYER

### Retina and Optic Nerve

ANGIOMATOSIS RETINAE (VON HIPPEL'S DISEASE) RESULTS FOLLOWING IRRADIATION OF THREE EYES F C CORDES and O C DICKSON, *Am J Ophth* 26: 454 (May) 1943

Cordes and Dickson supply the following summary

"Three eyes of two patients with angiomatosis retinae were irradiated. In the first patient, who had an early lesion in one eye, there was a marked improvement with retention of 0.8 vision, 3½ years after irradiation. In the second case both eyes were involved, the right eye being in a well-advanced stage, whereas the lesion in the left eye was an early one. Both eyes were given 1,800 r. The early lesion showed definite improvement in vision of 10 two years after irradiation. During this time the eye having the more advanced lesion became progressively worse, going on to amaurosis, complete detachment of the retina, and gliosis

"From our experience with three eyes and from what is reported in the literature it appears that in early cases X-ray therapy does offer a convenient, safe means of treating these lesions. The advanced lesions have not responded to any type of therapy

"Electrolysis, diathermy, radium, and x-ray irradiation have all been used with success. It seems worthwhile to record the results obtained so that at a later date it may be possible to

evaluate better the various methods now employed in the treatment of this rare disease"

The article is illustrated W ZENTMAYER

CONCERNING DETACHMENT OF THE RETINA H S GRADLE, *Am J Ophth* 26: 524 (May) 1943

Gradle records an interesting case of detachment of the retina occurring in a woman aged 43. Preoperative immobilization of the patient for five to ten days is advised. The position of the patient must be maintained until the surgical procedure is completed. During the latter half of the operation the cornea frequently becomes hazy, so that the necessary view of the fundus is obscured. This was found to be due to pronounced increase in the tension of the eye. The haze disappeared within a few minutes after the final perforating puncture had been made. The hypertension is due to the shrinkage of the sclera by diathermy cauterization, with resultant decrease in the total volume capacity of the eyeball

W ZENTMAYER

### Tumors

GLIOMA OF THE RETINA IN SUCCESSIVE GENERATIONS W L BENEDICT and E M PARK-HILL, *Am J Ophth* 26: 511 (May) 1943

In 2 of the 4 cases of glioma of the retina reported the tumor occurred in successive generations. The mother of the patient in case 1 had had a glioma of the right eye at the age of 7 months. The diagnosis of the daughter's lesion was confirmed by microscopic examination. The patients in cases 2 and 3 were twin sisters, and the patient in case 3 subsequently gave birth to a daughter (case 4) who had bilateral glioma of the retina at the age of 2 years and 4 months

In all 4 cases the diagnosis was confirmed by microscopic examination. The disease was bilateral in cases 1, 3 and 4. In case 2 there was still no evidence of tumor in the right eye at the time of the patient's death

W ZENTMAYER

GLIOMA OF THE RETINA. A REVIEW OF TWELVE CASES W B E MCCREA, *Brit J Ophth* 27: 259 (June) 1943

McCrea summarizes his clinicopathologic study of 12 patients with so-called glioma of the retina who were treated at the Royal Victoria Eye and Ear Hospital during the period from 1938 to 1942 inclusive

*Incidence*—This series of 12 patients represents an incidence of 1 in a hospital population of 6,126, or 0.0017 per cent. This value is rather lower than has usually been reported in the literature—0.04 to 0.01 per cent (0.009 per cent in forty years at Innsbruck, as reported by Badtke)

*Age*—Two thirds of the patients were 3 years old or under when they came under observation,



the ages of the others being 8 (seen originally at the age of 1 year and 10 months),  $3\frac{1}{2}$ ,  $4\frac{1}{2}$  and 67 years respectively. The age of the last patient appears to constitute a record—48 years (Verhoeff) and 66 and 35 years (Gerald and Morel) being the highest previously reported.

*Sex*—Eight patients were males and 4 females. The figures in the literature indicate that the sexes are affected in about equal numbers.

*Heredity*—For none of the patients was it possible to trace any hereditary factor.

*Eyes Involved*—The disease was bilateral in 3 patients and unilateral in 9 patients.

*Trauma*—Two patients had a history of trauma.

*Mortality and Recovery*—Of the 12 patients 5 were known to have died, 1 could not be traced and was presumed to be dead, and 6 were alive and well at the time of the report, the periods varying from four years to four months since excision of the eye. The time elapsing between the diagnosis and removal of the eye and the patient's death was seven months for patient 1, nine months for patient 2, ten months for patient 6, nine years for patient 7 and five months for patient 8.

*Condition of the Optic Nerve and Extraocular Extension*—In only 1 globe (patient 8) was extraocular extension demonstrated. In patients 1 and 2 invasion of the orbital tissue was proved microscopically. The fifth patient was of particular interest in that there was invasion of the optic nerve, as far as the lamina cribrosa, with recovery, the patient being in good health three and a half years later (three years being generally regarded as the length of time necessary before a cure can be regarded as having taken place).

All the patients with involvement of the optic nerve outside the lamina cribrosa died.

*Type of Tumor*—Eleven patients had retinoblastoma, 5 of whom died, and 1 had a neuroepithelioma and was alive six months after operation. Parkell and Benedict, in a review of 16 cases each of retinoblastoma and neuroepithelioma in which they had been able to trace the patient, found good results in 12.6 and 62.5 per cent respectively. Badtke, in a review of the cases of glioma at Innsbruck from 1900 to 1939, expressed the opinion that the chance of cure was from 50 to 60 per cent. He placed the rate of recovery in the cases of bilateral glioma at 33 per cent. All the patients with bilateral glioma at the Royal Victoria Eye and Ear Hospital died.

W ZENTMAYER

ANGIOMA OF THE RETINA. A. G. CROSS, Brit J Ophth 27: 372 (Aug) 1943.

The case reported here is of interest as demonstrating a retinal angioma without the excessive gliosis which is characteristic of the condition

described by von Hippel. In a woman aged 29 the left eye presented a gray swelling adjoining the nasal margin of the disk. Several dilated veins were present over this tumor. Above and to the nasal side of the swelling there were about half a dozen red spots, which appeared to be retinal hemorrhages. As the lesion increased in size, the original diagnosis of congenital malformation was changed to that of probable malignant growth, and the eye was excised. Pathologic examination revealed a vascular formation at the junction of the retina and the optic disk, invading the optic nerve but not the choroid. There were endothelium-lined channels containing red blood corpuscles and varying in size from capillaries to vessels as large as the main branches of the central artery and vein. The supporting framework contained glia cells.

The article is illustrated. W ZENTMAYER

### Vision

ORTHOPTICS. EDUCATION IN BINOCULAR SKILL. J. E. LANCASTER, Am J Ophth 26: 463 (May) 1943.

Lancaster reaches the following conclusions:

"Orthoptics is not exercising the ocular muscles, it is not even primarily a procedure designed to straighten the eyes. It is the teaching of a patient to use his two eyes together for comfortable binocular vision. The emphasis in such training is the teaching of a skill in the use of unskilled neuromuscular coordination. Orthoptics will be of much greater value to physicians and their patients when its function is re-evaluated, not as primarily concerned with anomalies of eye position, but as devoted to helping the patient learn comfortable binocular visual habits."

W ZENTMAYER

### Therapeutics

IONTOTHERAPY (IONIC MEDICATION, IONTOPHORESIS, IONISATION) AS AN AID IN OPHTHALMIC THERAPEUTICS. N. FLEMING, Brit J Ophth 27: 354 (Aug) 1943.

Fleming describes the technic and the various agents employed by him in this form of therapy. He summarizes his results as follows:

"The principal feature of treatment by iontotherapy is reduction of congestion and so of inflammation generally.

"It is therefore of use in all forms of conjunctivitis.

"Cases are described showing remarkable success even in the treatment of such deep inflammations as scleritis, irido-cyclitis and retro-bulbar neuritis.

"These claims are based on experience gained in the treatment of some thousand cases, during the last ten years, both in hospital and private practice.

"Iontotherapy is likely to be of particular value in the treatment of war casualties."

W ZENTMAYER



## Book Reviews

**Virus Diseases in Man, Animal and Plant.** By Gustav Seiffert English translation by Marion Lee Taylor, Ph D Price, \$5 Pp 323, with 7 illustrations New York Philosophical Library, Inc, 1944

The author states in his preface that it is his purpose to furnish an introduction to the field of virus diseases by reviewing the most recent literature and by summarizing the present status of virus investigation. He points out, quite rightly, that recent surveys of the whole field, or of its parts, have been full of gaps. It is unfortunate, therefore, that his book, while offering a valuable survey of certain aspects of the subject, is itself full of gaps and in general disappointing. The translator is evidently unfamiliar with virus terminology, and what appears to have been an attempt at literal translation has led to some all but unintelligible passages. There are also innumerable errors in spelling and punctuation, evidence of a regrettable lack of care in proofreading.

Workers in this field will find valuable the first section, of ninety pages, which presents a general consideration of virus diseases. The second section consists of reviews of the individual virus diseases, and many of these seem unnecessarily short and incomplete. This is particularly true with respect to the virus diseases of ophthalmologic importance, herpes simplex being the only one receiving any sort of adequate treatment. Perhaps the diseases most poorly treated are trachoma and inclusion blennorrhoea, the latter being called, by some error of the translator or the author, "trachoma of the conjunctivae." While the author claims to cover the major research of the last decade, no ref-

erence is made to the numerous and valuable studies on trachoma by Julianelle and his associates.

The third part of the volume is concerned with virus-like agents, including the rickettsias and the organisms of pleuropneumonia. The fourth part deals with filtrable forms of bacteria. The concluding section summarizes the methods of virus investigation and is the part which, perhaps, will be most valuable to the student of viruses.

It is unfortunate that a work so needed, and potentially so valuable, should be marred by such poor composition and by so many omissions.

PHILLIPS THYGESON

**Transactions of the American Ophthalmological Society** Volume 41 Pp 628 Philadelphia American Ophthalmological Society, 1943

This volume brings the activities of the society at the annual meeting at Hot Springs, Va., June 10, 11 and 12, 1943, with Dr H H McGuire, president, in the chair. Twenty-two papers were read and discussed. The subjects ranged from the intracapsular cataract operation, keratoconjunctivitis sicca, distribution of certain oxidative enzymes in the ciliary body, split macula, retinal detachment and trauma, hypertensive diseases, pigment freckles of the iris and traumatic enophthalmos to choked disk and low intrathecal pressure. There are, in addition, six obituaries and the theses of nine successful candidates.

The editor, Dr Wilfred E Fry, of Philadelphia, deserves great praise for the excellent appearance of this volume.

ARNOLD KNAPP

## News and Notes

### GENERAL NEWS

**American Board of Ophthalmology**—Examinations during 1945 have been tentatively scheduled for the following months in the cities mentioned, the program being contingent on war and transportation conditions.

Los Angeles in January during the midwinter course, provided the number of applicants warrant it. Applications should be in hand by October 1.

New York in June. The exact dates will be announced about January 1. Applications should be sent in by December 1.

Chicago in October. The exact dates will be announced later. Applications should be in hand by April 1.

The executive office of the board has been changed to Cape Cottage, Maine, and all correspondence should be sent to that address.

The third edition of the "Directory of Medical Specialists," listing the names of and biographic data on all persons certified by the fifteen American boards is to be published early in 1945. Collection of biographic data for the diplomates certified since the 1942 edition and revision of the older listings in that volume are now going forward rapidly. Diplomates are requested to make prompt return of the data regarding their biographies as soon as possible after receiving the proper forms from the publication office soon to be mailed to them.

# Directory of Ophthalmologic Societies \*

## INTERNATIONAL

### INTERNATIONAL ASSOCIATION FOR PREVENTION OF BLINDNESS

President Dr P. Baillart, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France

Secretary-General Prof M Van Duyse, Université de Gand, Gand, Prov Ostflandern, Belgium

All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France

### INTERNATIONAL OPHTHALMOLOGIC CONGRESS

President Prof Nordenson, Serafimerlasarettet, Stockholm, Sweden

Secretary Dr Ehlers, Jerbanenegade 41, Copenhagen, Denmark

### INTERNATIONAL ORGANIZATION AGAINST TRACHOMA

President Dr A F MacCallan, 17 Horseferry Rd, London, England

### PAN-AMERICAN CONGRESS OF OPHTHALMOLOGY

President Dr Harry S Gradle, 58 E Washington St, Chicago

Executive Secretaries Dr Conrad Berens, 35 E 70th St, New York Dr M E Alvaro, 1511 Rua Consolidação, São Paulo, Brazil

## FOREIGN

### ALL-INDIA OPHTHALMOLOGICAL SOCIETY

President Dr B K Narayan Rao, Minto Ophthalmic Hospital, Bangalore

Secretary Dr G Zachariah, Flitcham, Marshall's Rd, Madras

### BRITISH MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President Dr W Clark Souter, 9 Albyn Pl, Aberdeen, Scotland

Secretary Dr Frederick Ridley, 12 Wimpole St, London, W 1

### CHENG TU OPHTHALMOLOGICAL SOCIETY

President Dr Eugene Chan

Secretary Dr K S Sun

Place Eye, Ear, Nose and Throat Hospital, Chengtu, China

### CHINESE OPHTHALMOLOGY SOCIETY

President Dr C H Chou, 363 Avenue Haig, Shanghai

Secretary Dr F S Tsang, 221 Foochow Rd, Shanghai

### CHINESE OPHTHALMOLOGICAL SOCIETY OF PEIPING

President Dr H T Pi, Peiping Union Medical College, Peiping

Secretary Dr C K Lin, 180 Hsi-Lo-yen Chienmeng, Peiping

Place Peiping Union Medical College, Peiping Time Last Friday of each month

### GERMAN OPHTHALMOLOGICAL SOCIETY

President Prof W Lohlein, Berlin

Secretary Prof E Engelking, Heidelberg

## HUNGARIAN OPHTHALMOLOGICAL SOCIETY

President Prof I Imre, Budapest

Assistant Secretary Dr Stephen de Grósz, University Eye Hospital, Máriautca 39, Budapest

All correspondence should be addressed to the Assistant Secretary

## MIDLAND OPHTHALMOLOGICAL SOCIETY

President Dr W Niccol, 4 College Green, Gloucester, England

Secretary Mr T Harrison Butler, 61 Newhall St, Birmingham 3, England

Place Birmingham and Midland Eye Hospital

## NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President Dr A MacRae, 6 Jesmond Rd, Newcastle-upon-Tyne, England

Secretary Dr Percival J Hay, 350 Glossop Rd, Sheffield 10, England

Place Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation Time October to April

## OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President Dr A James Flynn, 135 Macquarie St, Sydney

Secretary Dr D Williams, 193 Macquarie St, Sydney

## OPHTHALMOLOGICAL SOCIETY OF EGYPT

President Prof Dr Mohammed Mahfouz Bey, Government Hospital, Alexandria

Secretary Dr Mohammed Khalil, 4 Baehler St, Cairo

All correspondence should be addressed to the secretary, Dr Mohammed Khalil

## OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President Mr T Harrison Butler, 61 Newhall St, Birmingham 3, England

Secretary Mr L H Savin, 7 Queen St, London, W 1, England

## OPHTHALMOLOGY SOCIETY OF BOMBAY

President Dr D D Sathaye, 127 Girgaum Rd, Bombay 4, India

Secretary Dr H D Dastur, Dadar, Bombay 14, India

Place H B A Free Ophthalmic Hospital, Parel, Bombay 12 Time First Friday of every month

## OXFORD OPHTHALMOLOGICAL CONGRESS

Master Mr P G Doyne, 60 Queen Anne St, London, W 1, England

Secretary-Treasurer Dr F A Anderson, 12 St John's Hill, Shrewsbury, England

Place Oxford, England Time July 8-9, 1943

## PALESTINE OPHTHALMOLOGICAL SOCIETY

President Dr Arich Feigenbaum, Abyssinian St 15, Jerusalem

Secretary Dr E Sinai, Tel Aviv

## POLISH OPHTHALMOLOGICAL SOCIETY

President Dr W Kapuściński, 2 Waly Batorego, Poznań

Secretary Dr J Sobański, Lindley'a 4, Warsaw

Place Lindley'a 4 Warsaw

\* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date

ROYAL SOCIETY OF MEDICINE, SECTION OF  
OPHTHALMOLOGY

President Col F A Juler, 96 Harley St, London,  
W 1, England  
Secretary Dr Harold Ridley, 60 Queen Anne St,  
London, W 1, England

SÃO PAULO SOCIETY OF OPHTHALMOLOGY

President Dr W Belfort Mattos, Caixa Postal, 4086,  
São Paulo, Brazil  
Secretary Dr Silvio de Almeida Toledo, Enfermaria  
Santa Luzia, Santa Casa de Misericórdia, Cesario  
Motta, St 112, São Paulo, Brazil

SOCIEDAD ARGENTINA DE OFTALMOLOGIA

Chairman Dr Jorge Malbrán, Buenos Aires  
Secretary Dr Benito Just Tiscornia, Santa Fe 1171,  
Buenos Aires

SOCIEDAD OFTALMOLOGIA DEL LITORAL,  
ROSARIO (ARGENTINA)

President Prof Dr Carlos Weskamp, Laprida 1159,  
Rosario  
Secretary Dr Juan M Vila Ortiz, Cordoba 1433,  
Rosario  
Place Rosario Time Last Saturday of every month,  
April to November, inclusive All correspondence  
should be addressed to the President

SOCIEDADE DE OPHTHALMOLOGIA E OTO-RHINO-  
LARYNGOLOGIA DA BAHIA

President Dr Theonilo Amorim, Barra Avenida,  
Bahia, Brazil  
Secretary Dr Adroaldo de Alencar, Brazil  
All correspondence should be addressed to the President

SOCIETA OFTALMOLOGICA ITALIANA

President Prof Dott Giuseppe Ovio, Ophthalmological  
Clinic, University of Rome, Rome  
Secretary Prof Dott Epimaco Leonardi, Via del  
Gianicolo, 1 Rome

SOCIÉTÉ FRANÇAISE D'OPHTHALMOLOGIE

Secretary Dr Rene Onfray, 6 Avenue de la Motte  
Picquet, Paris, 7<sup>e</sup>

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President Prof K G Ploman, Stockholm  
Secretary Dr K. O Granstrom, Sodermalmstorg 4  
III tr, Stockholm, Sö

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President Dr D Arieh-Friedman, 96 Allenby St, Tel  
Aviv, Palestine.  
Secretary Dr Sadger Max, 9 Bialik St, Tel Aviv,  
Palestine

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC  
ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman Dr Frederick C Cordes, 384 Post St, San  
Francisco  
Secretary Dr R. J Masters, 23 E. Ohio St, Indian-  
apolis

AMERICAN ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President Dr Lawrence T Post, Metropolitan Bldg,  
St Louis  
President-Elect Dr Gordon B New, Mayo Clinic,  
Rochester, Minn  
Executive Secretary-Treasurer Dr William L Bene-  
dict, 101-1st Ave Bldg, Rochester, Minn

AMERICAN OPHTHALMOLOGICAL SOCIETY

President Dr S Judd Beach, 704 Congress St, Port-  
land, Maine  
Secretary-Treasurer Dr Walter S Atkinson, 129  
Clinton St, Watertown, N Y

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC

Chairman Dr Frederick C Cordes, 384 Post St San  
Francisco  
Secretary-Treasurer Major Brittain F Payne, School  
of Aviation Medicine, Randolph Field, Texas

CANADIAN MEDICAL ASSOCIATION, SECTION ON  
OPHTHALMOLOGY

President Dr Alexander E MacDonald, 170 St George  
St, Toronto  
Secretary-Treasurer Dr L J Sebert, 170 St George  
St, Toronto

CANADIAN OPHTHALMOLOGICAL SOCIETY

President Dr R Evatt Mathers, 34½ Morris St,  
Halifax, N S  
Secretary-Treasurer Dr Kenneth B Johnston, Suite 1  
1509 Sherbrooke St W, Montreal  
Place Halifax, N S Time Aug 4-5, 1944

NATIONAL SOCIETY FOR THE PREVENTION OF  
BLINDNESS

President Mr Mason H Bigelow, 1790 Broadway,  
New York.  
Secretary Miss Regina E Schneider, 1790 Broadway,  
New York  
Executive Director Mrs Eleanor Brown Merrill, 1790  
Broadway, New York

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY,  
SECTION ON EYE, EAR, NOSE AND THROAT

President Dr N Zwaifler, 46 Wilbur Ave, Newark  
Secretary Dr William F Keim Jr, 25 Roseville Ave,  
Newark  
Place 91 Lincoln Park South, Newark Time 8 45  
p m, second Monday of each month, October to May

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr L J Friend, 425 E Grand Ave, Beloit,  
Wis  
Secretary Dr G L McCormick, 626 S Central Ave,  
Marshfield

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President Dr Paul A Chandler, 5 Bay State Rd,  
Boston  
Secretary-Treasurer Dr Merrill J King, 264 Beacon  
St, Boston  
Place Massachusetts Eye and Ear Infirmary, 243  
Charles St, Boston Time 8 p m, third Tuesday of  
each month from November to April, inclusive

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President Dr D H O'Rourke, 1612 Tremont Pl,  
Denver  
Secretary-Treasurer Dr C Allen Dickey, 450 Sutter  
St, San Francisco

PUGET SOUND ACADEMY OF OPHTHALMOLOGY  
AND OTO-LARYNGOLOGY

President Dr L L Bull, 1215-14th Ave, Seattle,  
Wash  
Secretary-Treasurer Dr Barton E Peden, 301 Stimson  
Bldg, Seattle 1  
Place Seattle or Tacoma, Wash Time Third Tues-  
day of each month except June, July and August

ROCK RIVER VALLEY EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr J Sheldon Clark, 27 E Stephenson St,  
Freeport, Ill  
Secretary-Treasurer Dr Harry R Warner, 321 W  
State St, Rockford, Ill  
Place Rockford, Ill, or Janesville or Beloit, Wis  
Time Third Tuesday of each month from October  
to April, inclusive

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr M H Pike, Midland, Mich  
Secretary-Treasurer Dr R H Criswell, 407 Phoenix  
Bldg, Bay City, Mich  
Place Saginaw or Bay City, Mich Time Second  
Tuesday of each month, except July and August

SIoux VALLEY EYE AND EAR ACADEMY

President Dr J C Decker, 515 Francis Bldg, Sioux  
City, Iowa  
Secretary-Treasurer Dr J E Dvorak, 408 Davidson  
Bldg, Sioux City, Iowa

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE,  
EAR, NOSE AND THROAT

Chairman Dr John H Burleson, 414 Navarro St,  
San Antonio, Texas  
Secretary Dr J W Jervey Jr, 101 Church St,  
Greenville, S C

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE  
AND THROAT

President Dr H L Brehmer, 221 W Central Ave,  
Albuquerque, N Mex  
Secretary Dr A E Cruthirds, 1011 Professional Bldg,  
Phoenix, Ariz

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President Dr W M Dodge, 716 First National Bank  
Bldg, Battle Creek  
Secretary-Treasurer Dr Kenneth Lowe, 25 W Mich-  
igan Ave, Battle Creek  
Time Last Thursday of September, October, Novem-  
ber, March, April and May

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr Ray Parker, 218 Franklin St, Johnston,  
Pa  
Secretary-Treasurer Dr J McClure Tyson, Deposit  
Nat'l Bank Bldg, DuBois

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR,  
NOSE AND THROAT SECTION

President Dr Raymond C Cook, 701 Main St, Little  
Rock  
Secretary Dr K W Cosgrove, Urquhart Bldg, Little  
Rock

COLORADO OPHTHALMOLOGICAL SOCIETY

President Dr C A Ringle, 912-9th Ave, Greeley  
Secretary Dr W A Ohmart, 1102 Republic Bldg,  
Denver  
Place University Club, Denver Time 7 30 p m,  
third Saturday of each month, October to May, in-  
clusive

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON  
EYE, EAR, NOSE AND THROAT

President Dr F L Phillips, 405 Temple St, New  
Haven  
Secretary-Treasurer Dr W H Turnley, 1 Atlantic  
St, Stamford, Conn

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President William O Martin Jr, Doctors Bldg,  
Atlanta  
Secretary-Treasurer Dr C K McLaughlin, 526  
Walton St, Macon

INDIANA ACADEMY OF OPHTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr F McK Ruby, Union City  
Secretary Dr Edwin W Dyar Jr, 23 E Ohio St,  
Indianapolis  
Place French Lick Time First Wednesday in April

IOWA ACADEMY OF OPHTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr J K Von Lackum, 117-3d St S E,  
Cedar Rapids  
Secretary-Treasurer Dr B M Merkel, 604 Locust St,  
Des Moines

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND  
OTOLARYNGOLOGICAL SOCIETY

President Dr Val H Fuchs, 200 Carondelet St, New  
Orleans  
Secretary-Treasurer Dr Edley H Jones, 1301 Wash-  
ington St, Vicksburg, Miss

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF  
OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr Robert H Fraser, 25 W Michigan  
Ave, Battle Creek  
Secretary Dr R G Laird, 114 Fulton St, Grand  
Rapids

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr George E McGeary, 920 Medical Arts  
Bldg, Minneapolis  
Secretary Dr William A Kennedy, 372 St Peter St,  
St Paul  
Time Second Friday of each month from October to  
May

## MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President Dr William Morrison, 208 N Broadway,  
Billings, Mont  
Secretary Dr Fritz D Hurd, 309 Medical Arts Bldg,  
Great Falls

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr W Howard Morrison, 1500 Medical  
Arts Bldg, Omaha  
Secretary-Treasurer Dr John Peterson, 1307 N St,  
Lincoln

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON  
OPHTHALMOLOGY, OTOTOLOGY AND  
RHINOLARYNGOLOGY

Chairman Dr B E Failing, 31 Lincoln Park, Newark  
Secretary Dr George Meyer, 410 Haddon Ave,  
Camden

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR,  
NOSE AND THROAT SECTION

Chairman Dr Harold J Joy, 504 State Tower Bldg,  
Syracuse 2  
Secretary Dr Maxwell D Ryan, 660 Madison Ave,  
New York 21

NORTH CAROLINA EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr Hugh C Wolfe, 102 N Elm St,  
Greensboro  
Secretary Dr Vanderbilt F Couch, 104 W 4th St,  
Winston-Salem

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY  
AND OTO-LARYNGOLOGY

President Dr W L Diven, City National Bank Bldg,  
Bismarck  
Secretary-Treasurer Dr A E Spear, 20 W Villard,  
Dickenson

OREGON ACADEMY OF OPHTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr Paul Neely, 1020 S W Taylor St,  
Portland  
Secretary-Treasurer Dr Lewis Jordon, 1020 S W  
Taylor St, Portland  
Place Good Samaritan Hospital, Portland Time  
Thrd Tuesday of each month

PENNSYLVANIA ACADEMY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr Lewis T Buckman, 83 S Franklin St,  
Wilkes-Barre  
Secretary Pro Tem Dr Paul C Craig, 232 N 5th  
St, Reading  
Time Last week in April

RHODE ISLAND OPHTHALMOLOGICAL AND  
OTOLOGICAL SOCIETY

Acting President Dr N Darrell Harvey, 112 Water-  
man St., Providence.  
Secretary-Treasurer Dr Linley C Happ, 124 Water-  
man St., Providence.  
Place Rhode Island Medical Society Library, Provi-  
dence Time 8 30 p m, second Thursday in  
October, December, February and April

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr J L Sanders, 222 N Main St, Green-  
ville  
Secretary Dr J H Stokes, 125 W Cheves St,  
Florence

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr Wesley Wilkerson, 700 Church St,  
Nashville  
Secretary-Treasurer Dr W D Stinson, 124 Physicians  
and Surgeons Bldg, Memphis

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL  
SOCIETY

President Dr F H Rosebrough, 603 Navarro St,  
San Antonio  
Secretary Dr M K McCullough, 1717 Pacific Ave,  
Dallas

## UTAH OPHTHALMOLOGICAL SOCIETY

President Dr R B Maw, 699 E South Temple, Salt  
Lake City  
Secretary-Treasurer Dr Charles Ruggeri Jr, 1120  
Boston Bldg, Salt Lake City  
Place University Club, Salt Lake City Time 7 00  
p m, thrd Monday of each month

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND  
OPHTHALMOLOGY

President Dr Mortimer H Williams, 30½ Franklin  
Rd S W, Roanoke  
Secretary-Treasurer Dr Meade Edmunds, 34 Franklin  
St, Petersburg

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE,  
EAR, NOSE AND THROAT SECTION

President Dr George Traugh, 309 Cleveland Ave,  
Fairmont  
Secretary Dr Welch England, 621½ Market St,  
Parkersburg

## LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr E L Mather, 39 S Main St, Akron,  
Ohio  
Secretary-Treasurer Dr V C Malloy, 2d National  
Bank Bldg, Akron, Ohio  
Time First Monday in January, March, May and  
November

## ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr B M Cline, 153 Peachtree St N E,  
Atlanta, Ga  
Acting Secretary Dr A V Hallum, 478 Peachtree  
St N E, Atlanta, Ga  
Place Grady Hospital Time 6 00 p m, fourth Mon-  
day of each month, from October to May

BALTIMORE MEDICAL SOCIETY, SECTION ON  
OPHTHALMOLOGY

Chairman Dr Ernst Bodenheimer, 1212 Eutaw Pl,  
Baltimore  
Secretary Dr Thomas R O'Rourke, 104 W Madison  
St, Baltimore  
Place Medical and Chirurgical Faculty, 1211 Cathedral  
St. Time 8 30 p m, fourth Thursday of each  
month from October to March

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President Each member, in alphabetical order.  
 Secretary Dr Luther E Wilson, 919 Woodward Bldg,  
 Birmingham, Ala  
 Place Tutwiler Hotel Time 6 30 p m, second  
 Tuesday of each month, September to May, inclusive

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President Dr William B Agan, 1 Nevins St, Brooklyn  
 Secretary-Treasurer Dr Benjamin C Rosenthal, 140  
 New York Ave, Brooklyn  
 Place Kings County Medical Society Bldg, 1313 Bed-  
 ford Ave Time Third Thursday in February, April,  
 May, October and December

BUFFALO OPHTHALMOLOGIC CLUB

President Dr Walter F King, 519 Delaware Ave,  
 Buffalo  
 Secretary-Treasurer Dr Sheldon B Freeman, 196  
 Linwood Ave, Buffalo  
 Time Second Thursday of each month

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND  
 OTOLARYNGOLOGY

President Each member, in alphabetical order  
 Secretary Dr Douglas Chamberlain, Chattanooga  
 Bank Bldg, Chattanooga, Tenn  
 Place Mountain City Club Time Second Thursday  
 of each month from September to May

CHICAGO OPHTHALMOLOGICAL SOCIETY

President Dr Vernon M Leech, 55 E Washington  
 St, Chicago  
 Secretary Dr W A Mann, 30 N Michigan Ave,  
 Chicago  
 Place Chicago Towers Club, 505 N Michigan Ave  
 Time Third Monday of each month from October  
 to May

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY  
 STAFF

Chairman Dr D T Vail, 441 Vine St, Cincinnati  
 Secretary Dr A A Levin, 441 Vine St, Cincinnati  
 Place Cincinnati General Hospital Time 7 45 p m,  
 third Friday of each month except June, July and  
 August

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman Dr Shandor Monson, 1621 Euclid Ave,  
 Cleveland  
 Secretary Dr Carl Ellenberger, 14805 Detroit Ave,  
 Cleveland  
 Time Second Tuesday in October, December, February  
 and April

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION  
 ON OPHTHALMOLOGY

Chairman Dr W S Reese, 1901 Walnut St,  
 Philadelphia  
 Clerk Dr George F J Kelly, 37 S 20th St,  
 Philadelphia  
 Time Third Thursday of every month from October  
 to April, inclusive

COLUMBUS OPHTHALMOLOGICAL AND OTO-  
 LARYNGOLOGICAL SOCIETY

Chairman Dr H D Emswiler, 370 E Town St,  
 Columbus, Ohio  
 Secretary-Treasurer Dr D G Sanor, 206 E State  
 St, Columbus, Ohio  
 Place The Neil House Time 6 p m, first Monday  
 of each month

CORPUS CHRISTI EYE, EAR, NOSE AND  
 THROAT SOCIETY

Chairman Dr Arthur Padillo, 414 Medical Profes-  
 sional Bldg, Corpus Christi, Texas  
 Secretary Dr Edgar G Mathis, 815 Medical Arts  
 Bldg, Corpus Christi, Texas  
 Time Second Friday of each month from October to  
 May

DALLAS ACADEMY OF OPHTHALMOLOGY AND  
 OTO-LARYNGOLOGY

President Dr Ruby K Daniel, Medical Arts Bldg,  
 Dallas 1, Texas  
 Secretary Dr Tom Barr, Medical Arts Bldg, Dallas 1,  
 Texas  
 Place Dallas Athletic Club Time 6 30 p m, first  
 Tuesday of each month from October to June The  
 November, January and March meetings are devoted  
 to clinical work

DES MOINES ACADEMY OF OPHTHALMOLOGY AND  
 OTOLARYNGOLOGY

President Dr H C Schmitz, 604 Locust St, Des  
 Moines, Iowa  
 Secretary-Treasurer Dr Byron M Merkel, 604 Locust  
 St, Des Moines, Iowa  
 Time 7 45 p m, third Monday of every month from  
 September to May

DETROIT OPHTHALMOLOGICAL CLUB

Chairman Dr Raymond S Goux, 545 David Whitney  
 Bldg, Detroit 26  
 Secretary Dr Arthur Hale, 1609 Eaton Tower, Detroit  
 Place Club rooms of Wayne County Medical Society  
 Time 6 30 p m, third Thursday of each month,  
 November through April

DETROIT OPHTHALMOLOGICAL SOCIETY

President Dr Parker Heath, 1553 Woodward Ave,  
 Detroit  
 Secretary Dr Leland F Carter, 1553 Woodward Ave,  
 Detroit  
 Place Club rooms of Wayne County Medical Society  
 Time Third Thursday of each month from Novem-  
 ber to April, inclusive

EASTERN NEW YORK EYE, EAR, NOSE AND  
 THROAT ASSOCIATION

President Appointed at each meeting  
 Secretary-Treasurer Dr Joseph L Holohan, 330 State  
 St, Albany  
 Time Third Wednesday in October, November, March,  
 April, May and June

FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Rex Howard, 602 W 10th St, Fort  
 Worth, Texas  
 Secretary-Treasurer Dr R H Gough, Medical Arts  
 Bldg, Fort Worth, Texas  
 Place Medical Hall, Medical Arts Bldg Time 7 30  
 p m, first Friday of each month except July and  
 August

# HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SECTION

President Dr Lyle J Logue, 1304 Walker Ave, Houston, Texas

Secretary Dr John T Stough, 803 Medical Arts Bldg, Houston, Texas

Place Medical Arts Bldg, Harris County Medical Society Rooms Time 8 p m, second Thursday of each month from September to June

## INDIANAPOLIS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President Dr Myron Harding, 23 E Ohio St, Indianapolis

Secretary Dr Kenneth L Craft, 23 E Ohio St, Indianapolis

Place Indianapolis Athletic Club Time 6 30 p m, second Thursday of each month from November to May

## KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Edgar Johnson, 906 Grand Ave, Kansas City, Mo

Secretary Dr W E Keith, 1103 Grand Ave, Kansas City, Mo

Time Third Thursday of each month from October to June The November, January and March meetings are devoted to clinical work

## LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr Harold Snow, 614 S Pacific Ave, San Pedro, Calif

Secretary-Treasurer Dr Oliver R Nees, 508 Times Bldg, Long Beach, Calif

Place Professional Bldg Time Last Wednesday of each month from October to May

## LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr M E Trainor, 523 W 6th St, Los Angeles

Secretary-Treasurer Dr Orrie E Ghrist, 210 N Central Ave, Glendale, Calif

Place Los Angeles County Medical Association Bldg, 1925 Wilshire Blvd Time 6 00 p m, fourth Monday of each month from September to May, inclusive

## LOUISVILLE EYE AND EAR SOCIETY

President Dr Joseph S Heitger, Heyburn Bldg, Louisville, Ky

Secretary-Treasurer Dr J W Fish, 321 W Broadway, Louisville, Ky

Place Brown Hotel Time 6 30 p m, second Thursday of each month from September to May, inclusive

## LOWER ANTHRACITE EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Each member in alphabetical order

Secretary Dr James J Monohan 31 S Jardin St, Shenandoah, Pa

## MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr P S Constantinople, 1835 I St N W, Washington

Secretary Dr Frazier Williams, 1801 I St N W, Washington

Place 1718 M St N W Time 8 p m, third Friday of each month from October to April, inclusive

## MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Each member in alphabetical order

Secretary Dr Sam H Sanders, 1089 Madison Ave, Memphis, Tenn

Place Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital Time 8 p m, second Tuesday of each month from September to May

## MILWAUKEE OTO-OPHTHALMIC SOCIETY

President Dr Edwin C Bach, 324 E Wisconsin Ave, Milwaukee

Secretary-Treasurer Dr Ralph T Rank, 238 W Wisconsin Ave, Milwaukee

Place University Club Time 6 30 p m, second Tuesday of each month

## MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman Dr H V Dutrow, 1040 Fidelity Medical Bldg, Dayton, Ohio

Secretary-Treasurer Dr Maitland D Place, 981 Reibold Bldg, Dayton, Ohio

Place Van Cleve Hotel Time 6 30 p m, first Tuesday of each month from October to June, inclusive

## MONTREAL OPHTHALMOLOGICAL SOCIETY

President Dr J Rosenbaum, 1396 Ste Catherine St W, Montreal, Canada

Secretary Dr L Tessier, 1230 St Joseph Blvd E, Montreal, Canada

Time Second Thursday of October, December, February and April

## NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr M M Cullom, 700 Church St, Nashville, Tenn

Secretary Dr R E Sullivan, 432 Doctors Bldg, Nashville, Tenn

Place St Thomas Hospital Time 8 p m, third Monday of each month from October to May

## NEW HAVEN OPHTHALMOLOGICAL SOCIETY

President Dr William H Ryder, 185 Church St, New Haven, Conn

Secretary Dr Frederick A Wiess, 255 Bradley St, New Haven, Conn

## NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr W B Clark, 1012 American Bank Bldg, New Orleans

Secretary Dr Mercer G Lynch, 1018 Maison Blanche Bldg, New Orleans

Place Louisiana State University Medical Bldg Time 8 p m, second Tuesday of each month from October to May

NEW YORK ACADEMY OF MEDICINE, SECTION OF  
OPHTHALMOLOGY

Chairman Dr Frank C Keil, 660 Madison Ave, New York  
Secretary Dr Willis S Knighton, 121 E 61st St, New York  
Time 8 30 p m, third Monday of every month from October to May, inclusive

NEW YORK SOCIETY FOR CLINICAL  
OPHTHALMOLOGY

President Dr Milton Berliner, 57 W 57th St, New York  
Secretary Dr Benjamin Esterman, 983 Park Ave, New York  
Place Squibb Hall, 745-5th Ave Time 8 p m, first Monday of each month from October to May, inclusive

OKLAHOMA CITY ACADEMY OF OPTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr James P Luton, 117 N Broadway, Oklahoma City  
Secretary Dr Harvey O Randel, 117 N Broadway, Oklahoma City  
Place University Hospital Time Second Tuesday of each month from September to May

OMAHA AND COUNCIL BLUFFS OPTHALMOLOGICAL  
AND OTO-LARYNGOLOGICAL SOCIETY

President Dr D D Stonecypher, Nebraska City, Neb  
Secretary-Treasurer Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha  
Place Omaha Club, 20th and Douglas Sts, Omaha  
Time 6 p m dinner, 7 p m program, third Wednesday of each month from October to May

PASSAIC-BERGEN OPTHALMOLOGICAL CLUB

President Dr Thomas Sanfacon, 340 Park Ave, Paterson, N J  
Secretary-Treasurer Dr J Averbach, 435 Clinton Ave, Clinton, N J  
Place Paterson Eye and Ear Infirmary Time 9 p m, last Friday of every month, except June, July and August

PHILADELPHIA COUNTY MEDICAL SOCIETY,  
EYE SECTION

President Dr Isaac Tassman, 136 S 16th St, Philadelphia  
Secretary Dr Glen Gregory Gibson, 255 S 17th St, Philadelphia  
Time First Thursday of each month from October to May

PITTSBURGH OPTHALMOLOGICAL SOCIETY

President Dr John B McMurray, 6 S Main St, Washington, Pa  
Secretary Dr George H Shuman, 351-5th Ave, Pittsburgh  
Place Pittsburgh Academy of Medicine Bldg Time Fourth Monday of each month, except June, July, August and September

READING EYE, EAR, NOSE AND THROAT SOCIETY

President Dr R M Brickbauer, Shillington, Pa.  
Secretary Dr Paul C Craig, 232 N 5th St, Reading, Pa  
Place Wyomissing Club Time 6 30 p m, third Wednesday of each month from October to July

RICHMOND OPTHALMOLOGICAL AND OTO-  
LARYNGOLOGICAL SOCIETY

President Dr Peter N Pastore, Medical College of Virginia, Richmond, Va  
Secretary Dr Clifford A Folkes, Professional Bldg, Richmond, Va  
Place Westmoreland Club Time 6 p m, second Monday of each month from October to May

ROCHESTER EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr Frank Barber, 75 S Fitzhugh St, Rochester, N Y  
Secretary-Treasurer Dr Charles T Sullivan, 277 Alexander St, Rochester, N Y

ST LOUIS OPTHALMIC SOCIETY

President Dr C C Beisbarth, 3720 Washington Blvd, St Louis  
Secretary Dr H R Hildreth, 508 N Grand Blvd, St Louis  
Place Oscar Johnson Institute Time Clinical meeting, 5 30 p m, dinner and scientific meeting 6 30 p m, fourth Friday of each month from October to April, inclusive, except December

SAN ANTONIO OPTHALMO-OTO-LARYNGOLOGICAL  
SOCIETY

President Dr Belvin Pritchett, 705 E Houston St, San Antonio 5, Texas  
Secretary-Treasurer Lt Col John L Matthews, AAF School of Aviation Medicine, Randolph Field, Texas  
Place San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center  
Time 7 p m, second Tuesday of each month from October to May

SAN FRANCISCO COUNTY MEDICAL SOCIETY,  
SECTION ON EYE, EAR, NOSE AND THROAT

Chairman Dr Roy H Parkinson, 870 Market St, San Francisco  
Secretary Dr A G Rawlins, 384 Post St, San Francisco  
Place Society's Bldg, 2180 Washington St, San Francisco  
Time Fourth Tuesday of every month except June, July and December

SHREVEPORT EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr David C Swearingen, Slattery Bldg, Shreveport, La  
Secretary-Treasurer Dr Kenneth Jones, Medical Arts Bldg, Shreveport, La  
Place Shreveport Charity Hospital Time 7 30 p m, first Monday of every month except July, August and September



SPOKANE ACADEMY OF OPHTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr Clarence A Veasey Sr, 421 W River-  
side Ave, Spokane, Wash  
Secretary Dr Clarence A Veasey Jr, 421 W River-  
side Ave, Spokane, Wash  
Place Spokane Medical Library Time 8 p m, fourth  
Tuesday of each month except June, July and August

SYRACUSE EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr A H Rubenstein, 713 E Genesee St,  
Syracuse, N Y  
Secretary-Treasurer Dr I H Blaisdell, 713 E  
Genesee St, Syracuse, N Y  
Place University Club Time First Tuesday of each  
month except June, July and August

TOLEDO EYE, EAR, NOSE AND  
THROAT SOCIETY

Chairman Dr E W Campbell, 316 Michigan St,  
Toledo, Ohio  
Secretary Dr L C Ravin, 316 Michigan St, Toledo,  
Ohio  
Place Toledo Club Time Each month except June,  
July and August

TORONTO ACADEMY OF MEDICINE, SECTION OF  
OPHTHALMOLOGY

Chairman Dr W R F Luke, 316 Medical Arts Bldg,  
Toronto, Canada  
Secretary Dr W T Gratton, 216 Medical Arts Bldg,  
Toronto, Canada  
Place Academy of Medicine, 13 Queens Park Time  
First Monday of each month, November to April

## WASHINGTON, D C, OPHTHALMOLOGICAL SOCIETY

President Dr S Bockoven, 1752 Massachusetts Ave,  
Washington, D C  
Secretary-Treasurer Dr John Lloyd, 1218-16th St  
N W, Washington, D C  
Place Medical Society of District of Columbia Bldg,  
1718 M St N W, Washington, D C Time 7 30  
p m, first Monday in November, January, March  
and May

## WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman Each member in turn  
Secretary Dr Samuel T Buckman, 70 S Franklin  
St, Wilkes-Barre, Pa  
Place Office of chairman Time Last Tuesday of  
each month from October to May

## CHRONIC KERATOCONJUNCTIVITIS ASSOCIATED WITH NOCARDIA

WILLIAM L. BENEDICT, M.D.\*

AND

HERMAN A. IVERSON, M.D.

Fellow in Ophthalmology, Mayo Foundation

ROCHESTER, MINN.

Reports on *Nocardia*, a subdivision of the genus *Actinomyces*, as a cause of disease of the eye are rarely found in the literature. A small number of cases of ocular infection due to *Streptothrix*, a synonym for *Actinomyces*, can be found. Various clinical observations have been made on streptotrichal infection of the eye. Superficial punctate keratitis,<sup>1</sup> yellowish nodules on the conjunctiva,<sup>2</sup> adherent yellowish white membrane on the palpebral conjunctiva<sup>3</sup> and raised nodules on the surface of the cornea or sclera<sup>4</sup> are a few of these. Although the usual infection lasts for years, 1 case was found in which streptotrichal infection of the eyes with adenitis and folliculosis lasted only three weeks.<sup>5</sup> Liégard and Landrieu<sup>6</sup> separated *Nocardia* from *Streptothrix foisteri* as a cause of chronic conjunctivitis with mucopurulent secretion. Cavara<sup>7</sup> summarized data on fungous infections of the eye.

### REPORT OF A CASE

The patient, a Saskatchewan woman 23 years old, was first seen at the Mayo Clinic in January 1940. The

\* Section on Ophthalmology, Mayo Clinic.

1 Bruce, G. M., and Locatcher-Khorazo, D. *Actinomyces*. Recovery of the *Streptothrix* in a Case of Superficial Punctate Keratitis, *Arch Ophth* **27** 294-298 (Feb) 1942.

2 Bakly. Three Cases of *Streptothrix* Infection of the Conjunctiva, *Tr Ophth Soc U Kingdom* **41** 521-525, 1921.

3 May, C. H., in discussion on Crigler, L. W. *Arch Ophth* **46** 171, 1917.

4 Sicardi, J. A., Regules, U., and Talice, R. V. Un cas intéressant d'actinomyose conjonctivo-sclérale d'origine traumatique, *Ann de parasitol* **14** 171-176 (March 1) 1936. Thies, O. Aktinomykose des Sehorgans, *Klin Monatsbl f Augenh* **86** 55-58 (Jan) 1931.

5 Knapp, A., and Dwyer, J. G. Acute *Streptothrix* Infection of the Conjunctiva, *Arch Ophth* **47** 497-499 (Sept) 1918.

6 Liégard and Landrieu. Un cas de mycose conjonctivale, *Ann d'ocul* **146** 418-426 (Dec) 1911.

7 Cavara, V. Ophthalmologisches. Le micosi oculari, *Zentralbl f d ges Ophth* **20** 718-720, 1928-1929.

disease in the eye had begun soon after an attack of scarlet fever at the age of 7 years. Episodes of ocular pain, lacrimation, photophobia, dimness of vision and injection of the conjunctivas, lasting from one to several weeks, had occurred. Between attacks a state of relative comfort and improved visual acuity had prevailed. Slight entropion began at the age of 17 years. Treatment with copper sulfate and sulfanilamide had been without effect on the chronic inflammation.

Examination at the clinic revealed visual acuity of 3/60 in the right eye and 6/10 in the left. The right eye showed divergence of 10 degrees. Puckering of the eyelids, due principally to photophobia, was present (fig 1A). A few cilia were directed inward, and a gelatinous grayish white discharge was present. The inner surfaces of the eyelids presented either large patches of bright red granulation tissue or patches of scar tissue (fig 1B and C). No true follicles or papillae were present. With the biomicroscope small arterial trees and also superficial bullae were seen on the bulbar conjunctiva. Both minute and gross bands of scar tissue divided the surfaces. Posterior symblepharon was present. There was moderate injection of both bulbar conjunctival and scleral vessels. The entire right cornea was involved in interstitial keratitis. Finely granular infiltration was present throughout, and there was gross as well as microscopic vascularization of all parts of the cornea (fig 1D). The vessels were just below Bowman's membrane in the central portion of the cornea, but at the limbus they were at all levels. Several dirty white deposits were present between larger loops of vessels in the center of the cornea. Except for two small vascularized nebulas near the periphery, the left cornea appeared normal (fig 1E).

The patient's condition has remained nearly stationary during the four years since she first came to the clinic. The corneal lesions have progressed slowly, and she has had almost constant irritation, photophobia and discharge from the eyes. Administration of sulfanilamide, potassium iodide, zinc sulfate and metaphen have failed to help her. The sodium salt of penicillin, 1,000 Oxford units per cubic centimeter of solution, was applied by drop every hour for two weeks when the patient was not asleep, without noticeable effect.

### BACTERIOLOGY

Eight cultures made at various intervals over a period of four years yielded, without fail, an organism which, according to the nomenclature

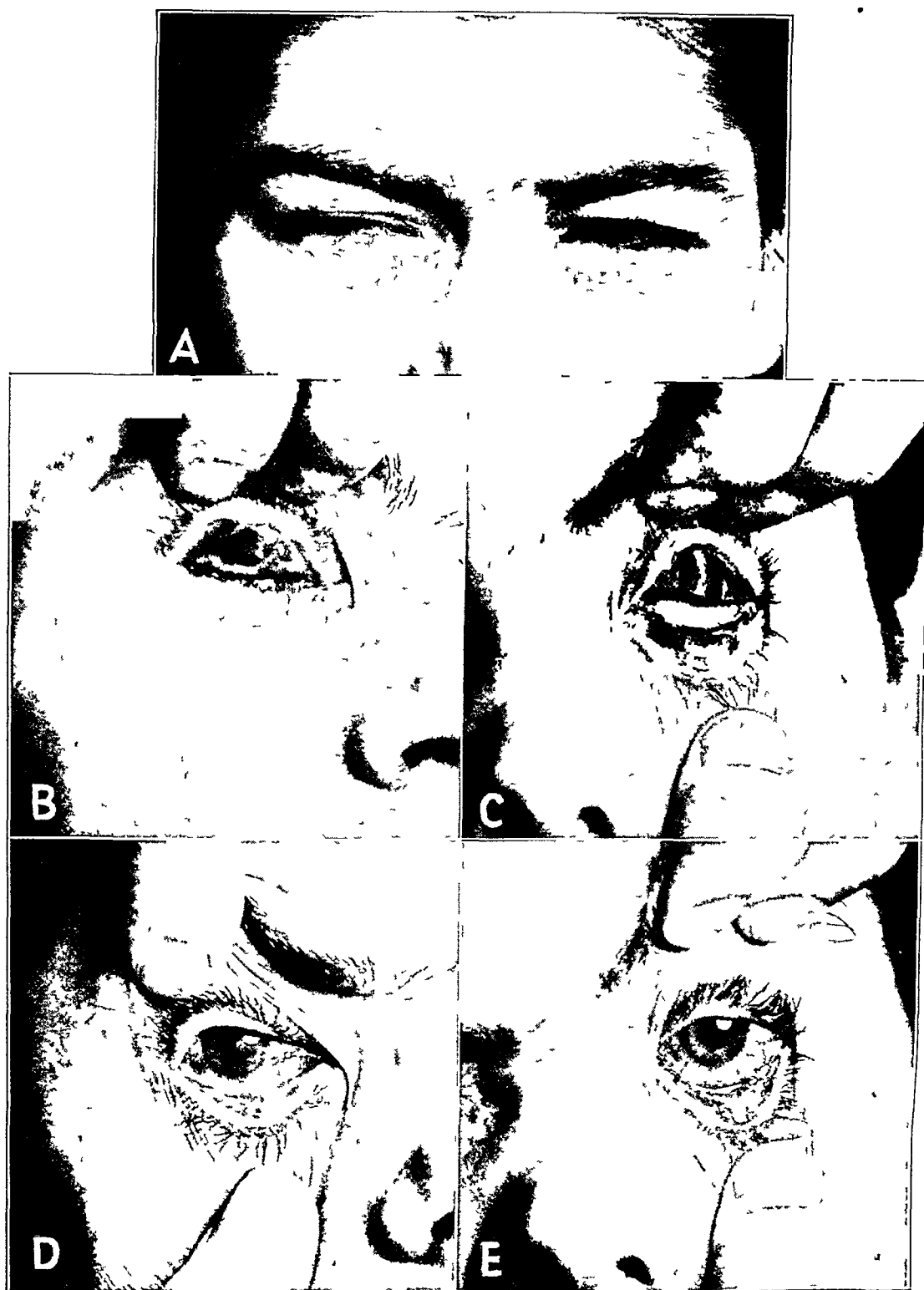


Fig 1—*A*, typical puckering of the eyelids *B*, right eye, with large patches of granulation tissue under the upper lid *C*, left eye, with regions of granulation tissue and scarring *D*, right eye, with infiltration and vascularization of the cornea, with small white deposits in the center *E*, left eye, with injection of bulbar conjunctival and scleral vessels

recommended by Waksman and Henrici,<sup>8</sup> should be classified as a *Nocardia*. Other organisms persistently found were alpha hemolytic streptococci, diphtheroid bacilli, micrococci and occasionally *Staphylococcus aureus*.

The *Nocardia* grew readily on all common laboratory mediums. On blood agar the surface colonies were roughly granular and had irregular edges (fig 2A). The umbonate shape is easily seen in figure 2A. The original light yellow

the bottom of the tube. After incubation for forty-eight hours, the surface film had climbed 6 mm up the sides of the tube. The surface glistened and appeared dry. After several days' growth, the film thickened and numerous deep yellow punctate accumulations appeared on the surface.

The organism, a gram-positive pleomorphic rod, was typically grouped in palisades in the fifteen hour broth culture (fig 2B). A typical

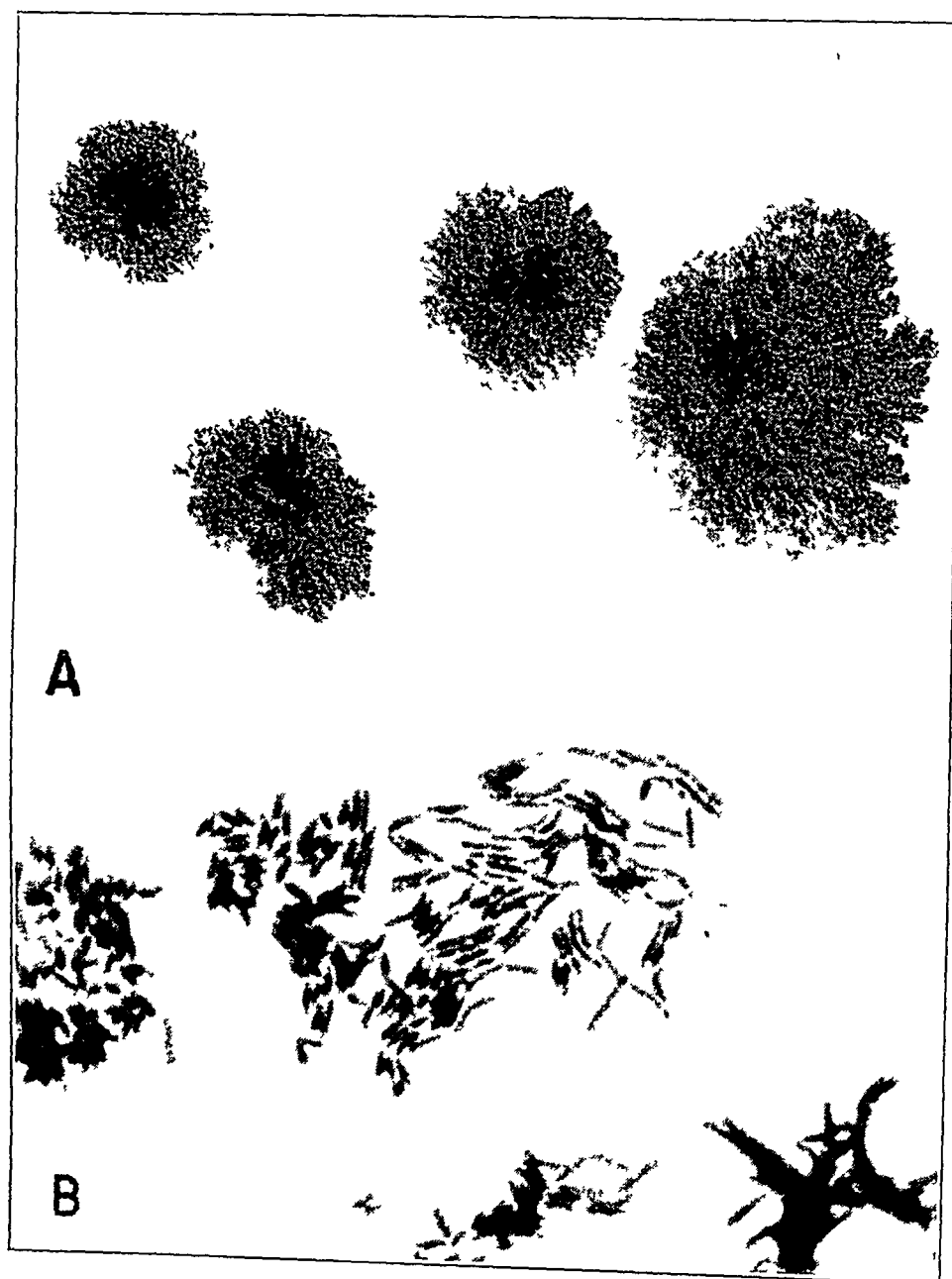


Fig 2—A, colonies of *Nocardia* on blood agar incubated at 37 C for three days ( $\times 6$ ). B, *Nocardia* organisms from a fifteen hour nutrient broth culture. The organisms are gram-positive ( $\times 2,000$ ).

color turned to a deep yellow after several weeks. When it was placed in a tube of nutrient broth, a thin yellowish film was found at the surface within six hours. Shaking the tube broke up the film into small particles, which would not remain in suspension but gradually settled to

the bottom of the tube. A mycelium was formed when the organism was incubated in a drop of plain nutrient agar between a cover slip and a glass slide. No branching or spores were seen under varying conditions. The mycelium always broke up into single rods when transferred to a slide for examination. Galactose, dextrose, sucrose, levulose and maltose were fermented, with formation of acid but not of gas. Salicin, inulin, raffinose, xylose and

<sup>8</sup> Waksman, S. A., and Henrici, A. T. The Nomenclature and Classification of the Actinomycetes, *J. Bact.* 46: 337-341 (Oct.) 1943.

lactose were not fermented. Gelatin stab cultures revealed good surface growth but no liquefaction after two weeks at 37 C. The catalase reaction was positive. The methyl red reaction was negative. Nitrates were converted to nitrites, with formation of the ammonium ion. The organism grew only between a  $p_H$  of 5.5 and 9.5. On litmus milk there was surface growth but no visible change in the medium. Indole was not converted to indigotin. There was no growth under anaerobic conditions. Yellowish punctate colonies were produced on washed potato. There was no coagulation of fresh human serum in four days and no liquefaction of coagulated horse serum in one week. It did not grow on Czapek's sucrose medium or with paraffin in Czapek's solution in one month. The organisms were not acid-fast when stained by the Ziehl-Neelsen method but were partially acid-fast to Umbreit's<sup>9</sup> modification of the stain. The sodium salt of penicillin diluted with nutrient broth to a concentration of 1 Oxford unit per cubic centimeter completely inhibited growth of the organism.

#### EXPERIMENTATION ON ANIMALS

Subcutaneous injection of living *Nocardia* organisms into a guinea pig, intravenous, intracerebral and intraperitoneal injections into mice and intravenous and intraperitoneal injections

into rabbits caused no morbidity. Necropsy of the guinea pig after one and a half months revealed nothing abnormal. Necropsy one week after intraperitoneal injection of the organisms into mice revealed a few white nodules in the spleens, pancreases and mesenteries. Microscopic sections of the lung of a rabbit after intravenous injection revealed a nonspecific foreign body reaction.

Living organisms were injected at several different times into the corneas and conjunctivas of a rabbit. Control injections of heat-killed organisms were made. There was little difference in the foreign body reaction caused by *the living and by the killed organisms*. Gradual absorption of the injected material was the rule.

#### COMMENT AND SUMMARY

Various unclassified types of *Actinomyces* are present in soil. The possibility of these organisms getting into the eyes is certainly not remote. Bakly stated that streptotrichal organisms are found on normal conjunctivas. It appears that the pathogenicity of this group of organisms is low and also that only a small percentage of persons are susceptible to this type of infection. When infection is once established, treatment is usually unsuccessful.

In this case the chronic keratoconjunctivitis was due, most likely, to a *Nocardia*. The bacteriologic studies contained herein were done in the laboratory of Dr. Fordyce R. Heilman.

<sup>9</sup> Umbreit, W. W. Studies on the Proactinomyces, *J. Bact.* **38** 73-89 (July) 1939.

# SARCOIDOSIS WITH RETINAL INVOLVEMENT

## REPORT OF TWO CASES

MAJOR S GOLDBERG\* AND LIEUTENANT F W NEWELL†

MEDICAL CORPS, ARMY OF THE UNITED STATES

Boeck's sarcoid was described by Longcope and Pierson<sup>1</sup> as "a chronic infectious granuloma, persisting often for years, sometimes spreading slowly from one organ or tissue of the body to another, frequently relapsing, seldom producing serious constitutional symptoms, resistant to treatment, but at times healing spontaneously." The most frequent site of ocular involvement is the iris. Blegvad<sup>2</sup> stated that iritis occurs in 10 per cent of the cases. Osterberg,<sup>3</sup> however, found but 27 cases of iritis in 500 cases of Boeck's sarcoid in the literature and estimated that involvement of the iris occurs in more nearly 5 per cent of the cases. The lacrimal gland and the conjunctiva are involved infrequently. The most uncommon sites of sarcoid infiltration are the choroid and the retina. King<sup>4</sup> stated that sarcoid must be considered as an extremely rare cause of localized chorioretinitis, an assertion which is definitely borne out by the scarcity of reported cases.

The earliest report of chorioretinitis accompanying Boeck's sarcoid is that of Hudelo and Rabut,<sup>5</sup> who described in 1925 a patient with the disease who presented iridocyclitis and bilateral choroiditis "*de nature bacillaire*." Reis and Rothfeld<sup>6</sup> in 1931 described a 17 year old white girl presenting cutaneous sarcoid of the Darier-Roussy type and roentgenographic evidence of osteitis cystica tuberculosa (Jungling) and of enlargement of the hilus glands. Exophthalmos and papilledema were present in both

eyes, together with secondary atrophy of the optic nerve in the right eye. The left eye presented a white tumor mass, elevated 20 diopters, with an uneven surface covered by retinal blood vessels. Vision was reduced to counting fingers at 40 cm with the right eye, and the left eye was blind. The patient died in an epileptiform attack, and necropsy revealed sarcoid involvement of the brain, the optic nerve and the left retina, with generalized tuberculosis elsewhere.

Horton, Lincoln and Pinner<sup>7</sup> described a white woman, aged 35, with recurrent uveitis in whom sarcoid changes were found in enlarged supraclavicular nodes removed for histologic study. The right eye showed evidence of previous iritis, and there were multiple inflammatory lesions in the lower half of the choroid with involvement of the overlying retina suggestive of tuberculosis. An exudate present in the pupillary area of the left eye prevented view of the fundus. Meyer<sup>8</sup> observed a patient, aged 24 with recurrent iritis and secondary glaucoma of the right eye and periphlebitis of the left inferior nasal vein with sarcoid present elsewhere.

Walsh<sup>9</sup> reported a white woman, aged 34, who showed blurring of the temporal margin of the optic nerve in the right eye, with slight pallor and numerous superficial, discrete white spots in the paramacular area, with a tendency to perivascular arrangement. The left eye showed white spots scattered throughout the fundus. One year later a mass, elevated 8 diopters, was present in the left eye and considered to be tuberculous. Nine years later the left eye was phthisic and was enucleated, sarcoid was demonstrated microscopically in the retina.

One of the 7 patients with Boeck's sarcoid reported by King<sup>4</sup> showed an active area of chorioretinitis in the left eye, which was healed two years later. King also examined an eyeball sent

\* Chief of Eye, Ear, Nose and Throat Section, LaGarde General Hospital

† Assistant chief of Eye, Ear, Nose and Throat Section, 108th General Hospital

1 Longcope, W T, and Pierson, W J. Boeck's Sarcoid, Bull Johns Hopkins Hosp 60 223, 1937

2 Blegvad, O. Boeck's Sarcoid der Conjunctiva, Acta ophth 9 180, 1931

3 Osterberg. Sarcoid of Boeck in Iritis, Brit J Ophth 23 145, 1939

4 King, M J. Ocular Lesions of Boeck's Sarcoid, Tr Am Ophth Soc 37 422, 1939

5 Hudelo and Rabut. Lupoides disseminées de Boeck, Bull Soc franç de dermat et syph 32 108, 1925

6 Reis, W, and Rothfeld, J. Tuberkulide des Sehnerven als Komplikation von Hautsarkoiden vom Typus Darier-Roussy, Arch f Ophth 126.357, 1931

7 Horton, R, Lincoln, N S, and Pinner, M. Noncascating Tuberculosis, Am Rev Tuberc 39 186, 1939

8 Meyer, F W. Augentuberkulose und Lymphogranulomatosis benigna, Klin Monatsbl f Augenh 102 76, 1939

9 Walsh, F B. Ocular Importance of Sarcoid, Arch Ophth 21 421 (March) 1939

to him for microscopic study and found typical sarcoid changes in the retina and in the distal portion of the optic nerve

Because of the scarcity of reported cases we believe it is of interest to report the following 2 cases which were observed during the past year at LaGarde General Hospital, New Orleans

**CASE 1**—A 23 year old Negro, single, was first seen Sept 4, 1942, complaining of painful swelling of the face and nodules in the inguinal region. He first noted nodular swelling in the right inguinal region June 25, 1942, which was followed by a similar swelling on the opposite side. About Aug 20, 1942, the parotid glands became moderately enlarged, and the posterior cervical, axillary, subclavicular and epitrochlear nodes became swollen. A marked diminution of vision in the right eye was noted at this time.

The family history was not relevant. There was no record of tuberculosis or venereal disease.

Physical examination revealed a moderately well nourished Negro, not acutely ill. The parotid glands and the lacrimal glands were somewhat enlarged and not tender. There was generalized, painless lymphadenopathy, with the nodes enlarged to the size of a lima bean. Neurologic examination revealed no abnormalities.

Vision in the right eye was reduced to perception of movements of the hands, and in the left eye was 20/20. The pupils were equal and reacted normally to light and in accommodation. Tension was 26 and 30 mm of mercury (McLean) in the right and the left eye respectively. Slit lamp examination showed no evidence of inflammation of the iris. There were much pigment and many blood cells in the anterior portion of the right vitreous. The right fundus showed numerous deep and superficial hemorrhages with thrombosis of the superior temporal vein, which had been replaced by a fibrous band. The arterioles were distinctly attenuated, and a severe edema was present in the macular area. The left fundus was normal.

Roentgenographic studies of the chest showed adenopathy of the hilar nodes of both lungs and a generalized increase of markings throughout both lung fields. No abnormalities of the bony structures of the hands or the feet could be demonstrated.

The blood showed a persistent hypochromic anemia, with the red cell count varying from 3,450,000 to 4,440,000 per cubic millimeter and the hemoglobin content varying from 63 to 74 Gm per hundred cubic centimeters. The white cell count varied from 3,450 to 8,750 per cubic millimeter, with eosinophils from 8 to 27 per cent. Cultures of blood and results of inoculation of guinea pigs with sputum were repeatedly negative. Repeated examinations of sputum revealed no acid-fast organisms. The Kahn and the Wassermann reactions were negative. Serum protein was 63 Gm per hundred cubic centimeters, with 255 Gm of albumin and 375 Gm of globulin. The sedimentation rate varied from 44 to 67 mm per hour. Agglutination tests with *Brucella melitensis* and *Pasteurella tularensis* gave negative results as did a cutaneous test with Frei antigen. The Mantoux reaction was negative with 1 mg of old tuberculin.

Repeated biopsies were made of enlarged nodes, and their microscopic appearances were similar. The normal structure of the lymph nodes was almost completely destroyed and replaced with numerous small tubercles. These were composed of epithelioid cells

without a zone of lymphoid tissue, with giant cells of the epithelioid type present. In a few tubercles under high power a small central portion of necrosis was seen. Boeck's sarcoid was the diagnosis of the pathologist (Major Sloan Wilson), and it was subsequently confirmed by the Army Histopathological Center.

Six weeks after the patient's admission a white mass, extending 3 diopters into the vitreous, was present at the inferior, nasal margin of the disk, and partially overlying it. The mass was superficial to the retinal blood vessels, of irregular surface, with many new blood vessels overlying it, and with sharply demarcated margins. The mass remained constant in size, and the vitreous cleared considerably in succeeding weeks, with all of the hemorrhages disappearing without sequela. A mass of new blood vessels extended from the disk forward into the vitreous, and the inferior nasal vessels were surrounded by whitish areas of retinal and choroidal destruction.

Early in the course of the disease the patient had a temperature never exceeding 100 F, which subsequently did not recur. The swelling of the parotid glands disappeared, the lymphadenopathy became much less severe and many nodes resolved spontaneously.

**CASE 2**—The patient, a 24 year old Negro soldier, married, was first seen Jan 27, 1943, complaining of swelling of the face and nodules in the arms and the forearms, which had been increasing in number the previous three months. He stated that after a hypodermic injection in September 1942 he noted "knotlike" nodules in the left forearm. In December 1942 swelling of the parotid glands developed, and he was hospitalized at a station hospital with the diagnosis of mumps. The swelling did not subside, and the patient was transferred to LaGarde Hospital.

The family history was not relevant and contained no record of tuberculosis. With the exception of pneumonia at the age of 12, the patient had had no previous illness.

Physical examination revealed a well nourished Negro, not acutely ill. The parotid glands were symmetrically enlarged, with nodules palpable immediately under the skin, and the indurated glands were felt beneath these. There was very slight tenderness to palpation. Deep in the subcutaneous tissue of the upper, outer angle of the orbits the size of a pea were palpated. The posterior cervical, subclavicular, epitrochlear and inguinal glands were slightly enlarged and felt like small, hard nodules. The arms and the forearms contained subcutaneous nodules, varying in size from that of a pea to that of an almond. The epithelium of the entire body was normal. Neurologic examination showed slight atrophy of the deltoid and the biceps muscles, with weakness in the left arm.

Vision in the right eye was 20/50, not improved with correction, and in the left eye 20/20. The pupils were equal and reacted normally to light and in accommodation. Tension was 20 and 24 mm of mercury (McLean) in the right and the left eye respectively. Slit lamp examination showed no evidence of involvement of the anterior segment. Ophthalmoscopic examination showed the right disk to be obscured in the inferior nasal quadrant by a grayish white mass approximately 2 disk diameters in size and extending nasalward. The mass was overlying the retinal blood vessels and projected 4 diopters into the vitreous. Numerous new blood vessels were present over the mass, which had sharp margins and was apparently encapsulated. Inferior and superior to the mass sub-

hyaloid hemorrhages were present. Small flame-shaped hemorrhages in the periphery and one adjacent to the macula were seen. The veins were of irregular caliber and constricted, the arterioles appeared normal.

Roentgenographic studies of the lungs revealed only an increase in the hilar markings. No pathologic condition of the phalanges could be demonstrated.

The white cell count varied between 5,300 and 10,950, with a normal differential count. Eosinophils never exceeded 3 per cubic millimeter. The red blood cell count varied between 4,600,000 and 5,600,000, with a hemoglobin content of 90 per cent. Urinalysis revealed no abnormality. The Wassermann and the Kahn reaction were negative on repeated examinations. The serum protein was 7.8 mg per hundred cubic centimeters, with 4 mg of albumin and 3.8 mg of globulin. The sedimentation rate was 79 mm per hour.

A cutaneous test for tuberculosis gave a negative reaction with 1 mg of old tuberculin. Agglutination tests with *P. tularensis* and *B. melitensis* gave negative results, as did a cutaneous test with Frei antigen.

Biopsy specimens were taken of a parotid gland, the right lacrimal gland and a subcutaneous nodule in the forearm. The report was essentially the same for each. The entire tissue was infiltrated with small lymphocytes and plasma cells, and there were numerous small tubercles present. These had an extremely narrow outer zone composed of fibrous tissue and lymphocytes, with a central area composed largely of fat cells, through which coursed small capillaries, with a few epithelial cells present. Each tubercle was moderately infiltrated with polymorphonuclear leukocytes, with no epithelial giant cells or foreign body giant cells present. There was a decided increase of connective tissue throughout the whole tissue. The histologic picture was such that it most nearly conformed with that of a sarcoid of the Darier-Roussy type.

The infiltration of each tubercle by polymorphonuclear leukocytes made the absolute diagnosis of sarcoid difficult. However, Colonel D. E. Ash of the Army Medical Center stated: "The histologic picture is distinctly atypical for an out and out diagnosis of sarcoid of the Darier-Roussy type, which, however, we favor against other possibilities." Microscopic sections of the biopsy specimens have been submitted to dermatopathologists throughout the country for opinions.

Five months after the onset of the swelling of the parotid glands the patient began to have almost daily slight hemoptysis, accompanied by gastrointestinal symptoms. Inoculation of sputum into a guinea pig gave negative results on two occasions. Repeated examinations of sputum and gastric washings did not reveal the presence of the tubercle bacillus. No pathologic condition of the intestinal tract could be demonstrated by roentgenograms, and studies of the stools revealed normal conditions. The swelling has remained constant, but there has been a slight decrease in the size of the subcutaneous nodules.

Vision in the right eye has improved to 20/30 without correction, and all hemorrhages have disappeared without residue. The mass overlying the disk has not increased in size, and new vascularization has apparently stopped.

The 2 cases reported have many of the clinical signs of sarcoid and are similar to each other in regard to the enlargement of the parotid and lacrimal glands, the numerous nodules over the forearms and the appearance of the fundi. The

initial diagnosis in the second case was made ophthalmoscopically, and we believe that possibly the lesions of the fundi in these cases are specific for sarcoidosis. The presence of these masses in the retina indicates the possibility that sarcoid may cause either an exudative ocular inflammation, as characterized by iritis, with or without an accompanying chorioretinitis, or a proliferative lesion, as occurred in these 2 cases. The masses observed in these cases probably represent a true sarcoid infiltration of the retinal tissue, as occurred in the cases of Reis and Rothfeld<sup>6</sup> and King,<sup>4</sup> in which the eyes were studied microscopically.

The retinal vascular changes are much more difficult to explain but may simply represent mechanical interference with the blood supply. However, in Meyer's<sup>8</sup> case the periphlebitis was a striking part of the ophthalmoscopic picture, and it may be, therefore, that the vascular changes are an essential part of the disease early in its course. In the first case here reported the vascular changes preceded the visible tumor mass, and possibly this sequence occurs in all cases of infiltration of sarcoid tubercles in the retina. Nothing specific for the disease was noted in the appearance of the fundi at this stage.

The infiltration of polymorphonuclear leukocytes in the nodules removed for microscopic study in case 2 is distinctly atypical and has made the absolute diagnosis of sarcoid difficult. However, clinically the case presents many of the symptoms and signs of sarcoid, and we believe that it represents a true instance of this disease.

Several considerations were essential before a diagnosis of sarcoidosis was made. Coats's disease, characterized by a massive exudation, with or without hemorrhages, occurring particularly in early adult life, bears some resemblance to the clinical picture visualized. In Coats's disease there is little or no generalized disorder. Cholesterol crystals are sometimes present.

Tuberculosis of the choroid of such extensive degree that a mass is present is practically always accompanied by anterior uveal involvement. Reactions to tuberculin were negative, negative reactions to tuberculin are the rule in sarcoidosis. Acute exudate choroiditis of more than moderate degree is usually accompanied by sufficient change in the aqueous to produce keratic precipitates. White blood cells in the vitreous are numerous. A blood dyscrasia or lymphosarcoma was a possible diagnosis, but each was eliminated by findings in the lymph nodes and by studies of the blood.

The condition in the second patient had been previously diagnosed as von Recklinghausen's disease, before he was admitted to LaGarde Gen-



eral Hospital. We did not see the very early stages, but at the time of admission the mass appeared to be overlying the retina, partially obscuring the disk. New vessels were seen passing over the edges, and anteriorly, as if the mass were encapsulated. The presence of widely spread nodules was suggestive of neurofibromatosis. However, clinical studies revealed evidence of sarcoidosis.

To recapitulate, in each of these cases whitish irregular masses, extending far forward into the vitreous, were present. Periphlebitis and hemorrhages were a prominent feature. In case 1 hemorrhage was extensive, both preretinally and in the retinal layers. There was absence of keratic precipitates, an optically clear aqueous and very little inflammatory response in the vitreous. The involved eye was always white. The formation of new blood vessels was strik-

ing early in the course of the disease, suggesting that the lesion would progress to a retinitis proliferans but with eventual absorption of the mass in each case. The retina remained in place. The end picture in each fundus was similar. There remained discrete whitish areas not unlike those seen after an exudative choroiditis.

No treatment was attempted in either case. Mydriatics were employed only for inspection.

#### SUMMARY AND CONCLUSION

Two cases of sarcoidosis with involvement of the retina are presented, the first an instance of the Boeck type and the second of an atypical, Darier-Roussy sarcoid. It is believed that the lesions of the fundi described may be specific for a proliferative type of sarcoid infiltration of the retina.

# WHITE RINGS OF THE CORNEA

## REPORT OF MICROSCOPIC EXAMINATION

M W JACOBY, M D, AND RAFAEL DOMINGUEZ, M D  
CLEVELAND

Only a small number of cases have been reported so far of the characteristic opacity of the cornea first described by Coats<sup>1</sup>. To the 42 cases collected by Bietti,<sup>2</sup> including 4 of his own, 2 cases of MacRae<sup>3</sup> and 5 of Waldman<sup>4</sup> may now be added.

In 46 of the 50 cases available, only one eye was affected and only one ring was present. One of Ballantyne's<sup>5</sup> patients had two rings in one cornea, 1 of Kuan's<sup>6</sup> had one ring in each cornea, 1 of MacRae's<sup>7</sup> had one ring in one cornea and several rings in the other cornea, and 1 of Coats's<sup>8</sup> had multiple rings in both eyes.

The rings occur in any part of the corneal field. By slit lamp examination the white deposit is seen in or adjacent to Bowman's membrane.

The rings cause no symptoms. As a matter of curiosity we should like to recall that 1 of the patients of Kuan<sup>6</sup> saw the white spot in the mirror and came to the clinic to have the "foreign body" removed.

The lesions are stationary for long periods. Waldman<sup>4</sup> did not notice any change in the lesions in 2 cases which he was able to observe for five and seven years respectively.

An idea of the rarity of the condition is given by Kuan,<sup>6</sup> who in two years found 11 cases of

the disease among 8,032 patients coming to the clinic for the first time. In an ophthalmologic practice extending over twenty years, one of us (M W J) has encountered only 5 cases.

Nothing is known concerning the cause of this lesion. Coats<sup>1</sup> expressed the opinion that it is congenital but brought no facts in support of this idea. Lampert,<sup>9</sup> Gallemaerts<sup>10</sup> and others stated the belief that the rings are produced by trauma. However, the frequency of the rings is exceptional when compared with the frequency of trauma to the eye (as pointed out by Bietti<sup>2</sup>), and in only 1 case has the ring been found within a nebula.<sup>3</sup> Ballantyne<sup>5</sup> and others remarked on the frequency with which the white rings are associated with either a previous history or the actual presence of some intraocular disease. Yet not 1 of the 11 patients of Kuan<sup>6</sup> had evidence of intraocular disease.

With regard to the pathogenesis of this lesion, two hypotheses have been advanced. Ballantyne,<sup>5</sup> after mentioning the drusen of Bowman's membrane described by Rindfleisch<sup>11</sup> and Elschnig,<sup>12</sup> suggested that the white rings could arise "from degenerative change, calcareous or otherwise, in such drusen." Kuan<sup>6</sup> stated the belief that the lesion is due primarily to a disease of the terminal branches of the corneal nerves and that this hypothetical disease may lead to a necrosis of Bowman's membrane, either by the action of some poison or by trophic disturbance. Kuan speculated further that the ring results from a secondary change—proteic precipitation, fatty degeneration or mineral incrustation—in the periphery of the necrosed part of Bowman's membrane.

9 Lampert, cited by Gallemaerts<sup>10</sup>. Of the cases cited by Gallemaerts, Ballantyne<sup>5</sup> retains only those of Lampert.

10 Gallemaerts, E. Examen microscopique des affections de la cornee au moyen de la lampe a fente, Paris, Masson & Cie, 1926.

11 Rindfleisch. Arch f Ophth **37** 236, 1891, cited by Ballantyne<sup>5</sup>.

12 Elschnig, A. Drusenbildung an der Bowman'schen Membran, Klin Monatsbl f Augenh **37**.453, 1899, cited by Ballantyne<sup>5</sup>.

From the Department of Ophthalmology and the Department of Pathology, St Luke's Hospital

1 Coats, G. Two Cases Showing a Small, Superficial, Opaque White Ring in the Cornea, Tr Ophth Soc U Kingdom **32**:53, 1912.

2 Bietti, G B. Sui cosiddetti anelli bianchi ("white rings, Coats") della cornea, Boll d'ocul **18** 907, 1939.

3 MacRae, A. "White Rings" in the Cornea, Tr Ophth Soc U Kingdom **55** 545, 1935.

4 Waldman, J. White Rings in Cornea (Coats), Am J Ophth **25** 1362, 1942.

5 Ballantyne, A J. "White Rings" in Cornea, Brit J Ophth **17**:336, 1933.

6 Kuan, K P. Ueber weisse Ringe in der Hornhaut, Arch f Ophth **135** 135, 1936.

7 MacRae, A. Cases of White Ring in the Cornea, Tr Ophth Soc U Kingdom **60**:234, 1940.

8 Coats, G. Small Superficial White Rings on the Cornea, Proc Roy Soc Med **7** 3, 1913.

The structure of the lesion is not well known. Only three authors have reported on the microscopic examination of excised rings.

Muramatsu,<sup>13</sup> according to Uyama,<sup>14</sup> found a homogeneous purple-staining substance under Bowman's membrane between this membrane and the substantia propria of the cornea. The epithelium, although thin, was intact and level over the opacity.

Uyama<sup>14</sup> removed the white ring of his patient with a needle and after fixing the piece of cornea with a solution of formaldehyde stained

to the zone containing the white ring. In the other 2 specimens, the result of the examination was rather meager. The only abnormalities mentioned consisted of a thinning of Bowman's membrane at some points, a lack of homogeneity of this membrane at some other points and, in 1 specimen, local disappearance of Bowman's membrane. Below Bowman's membrane Bietti noticed a few newly formed cellular elements, which he interpreted as connective tissue elements, and also a few masses of an amorphous degenerated tissue resembling hyalin.

We have had the opportunity of examining one of these rings after enucleation of the eye for some other condition. In view of the incomplete knowledge of both the structure and the chemical composition of this rare opacity, we think the report of our examination is of interest.

#### REPORT OF A CASE

A 55 year old Italian laborer came to the ophthalmic clinic May 1 1936 with the complaint of poor vision.

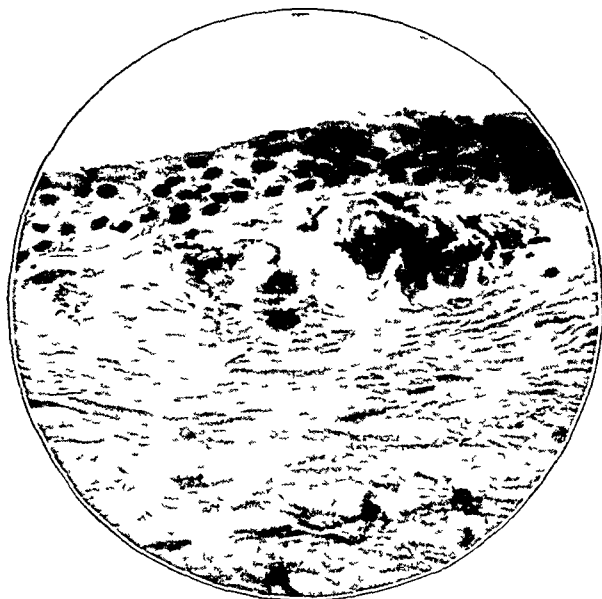


Fig 1 — Photomicrograph of a section of cornea (hematoxylin and eosin,  $\times 320$ ) showing the part of the ring farthest from the limbus.

it with sudan III. With the microscope he saw a small mass of orange-yellow granules in the superficial layer of the cornea. Uyama concluded that the white rings are certainly composed of fat. Since a nuclear stain was not used he could not determine the relation of the granules either to the epithelium or to Bowman's membrane.

Bietti<sup>2</sup> took biopsy specimens of the rings of 3 of his 4 patients. The specimens were fixed in a solution of formaldehyde, embedded in gelatin, sectioned and examined for fat. In only 1 of the 3 biopsy specimens was there a lipoid infiltration of Bowman's membrane, but this infiltration was rather diffuse and by no means confined

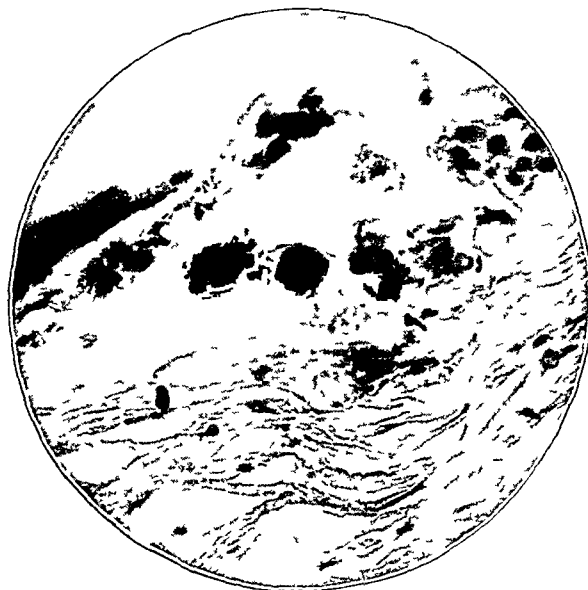


Fig 2 — Photomicrograph of the same section of cornea as in figure 1 showing the part of the ring nearest the limbus. The tear of the tissue is undoubtedly due to the brittleness of the cluster.

Vision was 6/30 in the right eye and 3/60 in the left eye. Examination disclosed immature cataracts, principally of a posterior saucer shape type, and hyperrefractive of the nucleus. No abnormalities were noticed in either fundus, but the details of the left were poorly seen.

External findings were unimportant with the exception of a white ring, 1 mm in diameter, located in the lower nasal quadrant of the right cornea near the limbus. With the corneal microscope the ring was seen to consist of conglomerate chalky dots located at the level of Bowman's membrane. Within the ring

13 Muramatsu, N. Five Cases of White Ring in Cornea, *Chuo-Ganka-Iho* 27:32, 1935, cited by Uyama.<sup>14</sup>

14 Uyama, Y. White Ring in Cornea. *Arch Ophth* 15:309 (Feb) 1936.

there were many discrete dots of the same character. The overlying epithelium was apparently normal, and the remainder of the cornea was also normal. There were no indications of previous disorder of the eye and no history of injury to the eye.

The results of a general physical examination were essentially normal. The upper right molar teeth presented periapical absorption and were extracted. A Wassermann test of the blood gave a negative result but the reaction to a Kline test was positive. Since no history and no signs of active syphilis were present no antisyphilitic treatment was advised at this time.



Fig 3—Photomicrograph of the same section of the cornea as in figures 1 and 2 showing the part of the cornea inside the ring

On Nov 2, 1936, a combined extraction was performed on the left eye, with no operative or postoperative complications. The ophthalmoscopic examination of this eye showed a clear vitreous and a normal fundus. Vision with correction was 6/6.

On June 17, 1938, a combined extraction was performed on the right eye, with no operative or postoperative complications. The ophthalmoscopic examination of the fundus disclosed no abnormalities. The vision in this eye was not corrected to better than 6/12.

On Jan 6, 1939, vision of the right eye was reduced to 6/24, the eye was quiet and a marked hypotony existed. A fairly clear view of the fundus showed no retinal detachment or evidence of a pathologic condition. An extremely thin capsular membrane was present but owing to the hypotony, dissection was not performed. The left eye was quiet and normal.

From the time of the first admission to the early part of 1939 all of seven Kline tests on the patient's blood gave positive results. The Wassermann test made at the same time gave positive results in three of the seven tests. In April 1939 the result of an examination of the spinal fluid was negative. The patient was considered to have latent syphilis and was treated rather lightly from April to October 1939.

(The patient's wife has been treated intensively for syphilis since 1929.)

On Feb 2, 1940, the patient reported to the clinic, stating that the right eye had been painful for several weeks. Vision was reduced to light perception, and there was distinct ciliary injection. The tension (Schiotz) was 33 mm of mercury. The iris was bulging forward, up to the posterior surface of the cornea, and obliterating the anterior chamber. The capsular membrane was also bulging forward, and a view of the fundus could not be obtained. The left eye was quiet, and the corneal microscope showed no evidence of inflammation of the eye.

Enucleation of the right eye was advised, and the eye was removed on Feb 27, 1940.

On the last examination, June 10, 1942, the serologic reactions of both blood and spinal fluid were negative.

*Microscopic Examination*—Immediately after enucleation, the cornea was excised and was fixed in dehydrated alcohol. After fixation, the part of the cornea containing the ring was embedded in paraffin and sectioned.

In the preparations stained with hematoxylin and eosin three clusters of bluish globules were seen. Two of these clusters lay just underneath the epithelium

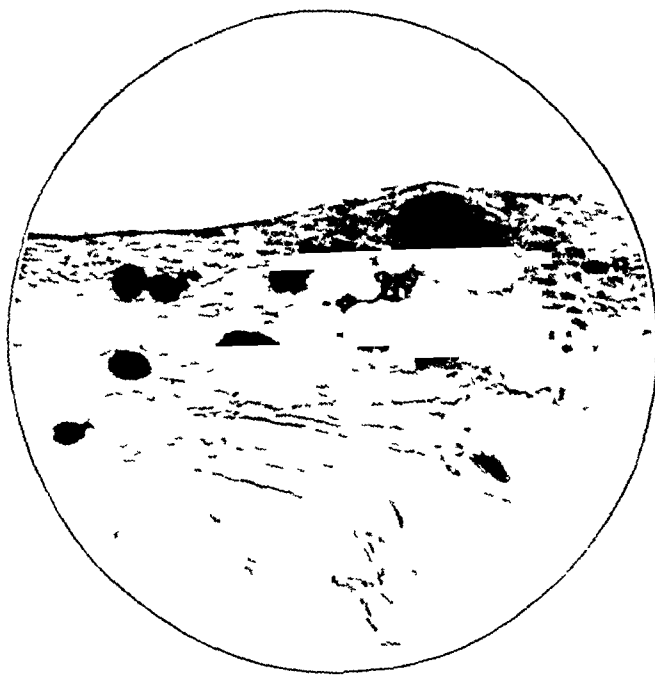


Fig 4—Photomicrograph of a section of cornea stained by Kossa's method ( $\times 320$ ). This is the only section of this cluster that did not tear.

(figs 1 and 2) and a third between the other two but deeper in the substance of the cornea (fig 3). The first two photomicrographs represent sections of the ring itself, and the third represents a section inside the ring. The globules were either circular or ovoid, and when ovoid the long axis was usually parallel to the surface of the cornea. The largest globule measured 31 microns in longest diameter and 19 microns in smallest diameter. The deepest surface of the deepest globule lay 64 microns below Bowman's membrane. A few of the globules could be located exactly in Bowman's membrane. (See, for instance, the globules

farthest to the left in figure 1) Others, especially those within the ring, lay clearly below Bowman's membrane and showed no connection with this membrane (fig 3) Still a few others were present above Bowman's membrane, actually within the epithelium (fig 4) The majority, however, lay in or adjacent to Bowman's membrane, corroborating the results of slit lamp examination No hyaline masses (drusen) were seen above Bowman's membrane either inside or outside the ring In the ring proper, where the deposit was heaviest, Bowman's membrane could not be seen, even after decalcification Figure 4 shows an elevation of the corneal surface on top of the cluster, but, since the cornea was not fixed in situ, this demonstration does not prove that the cornea was deformed before enucleation

The material of the globules is not homogeneous and in some a definite crystalline arrangement can be



Fig 5 — Photomicrograph of the same section as figures 1, 2 and 3 after decalcification and restaining (showing the same field reproduced in figure 1)

seen After treatment with a dilute solution of acetic acid the globules practically disappeared In sections treated by Kossa's method the globules became deep black (fig 4)

The section from which the first three photomicrographs were made was subsequently treated with potassium ferrocyanide and hydrochloride acid as a test for iron The globules were almost dissolved out without the formation of prussian blue The section was then restained with hematoxylin and eosin This time the clusters appeared as indistinct masses of a faintly stained amorphous material Directly above the remnants of the cluster reproduced in figure 1, there were found several elongated nuclei, which stained with hematoxylin fully as deeply as the nuclei of the overlying epithelium but more deeply than the nuclei of the corneal corpuscles (fig 5) By comparing figure 5 with figure 1, one can see that these nuclei were visible

in the original cluster before decalcification, but we could not identify them In all probability these filaments represented the deformed nuclei either of connective tissue cells, as suggested by Bietti, or of wandering cells immobilized in the neighborhood of the calcific deposits No other foreign cellular elements were seen, and no vascularization of the cornea was found

The sections of the globe after fixation in solution of formaldehyde and embedding in paraffin showed the usual appearance of secondary glaucoma without inflammation of the vascular membrane

#### COMMENT

From the foregoing examination it appears that the deposits forming the white rings contain calcium phosphate and no iron Other substances are undoubtedly present because the clusters do not disappear completely under the action of acids Our examination does not allow us to assert either the presence or the absence of lipids, but the report of Bietti<sup>2</sup> indicates that lipids are not a constant constituent of the rings In regard to the examination for calcium it is well to remember that practically all fixatives—except dehydrated alcohol—remove calcium from the tissues Indeed, it is possible that by using a solution of formaldehyde as a fixative Bietti may have removed a great deal of the calcium present in his biopsy specimens Otherwise it is difficult to reconcile the sharpness of the deposits seen both in vivo and in vitro (figs 2 and 3) with the vagueness of Bietti's findings But it is not difficult to reconcile the latter with the appearance of one of our decalcified clusters (fig 5)

Our results lend no support to the speculative views of either Ballantyne<sup>5</sup> or Kuan<sup>6</sup> concerning the pathogenesis of the deposit In areas of heavy calcareous deposit, Bowman's membrane is of course disorganized or even absent, but there are no drusen either outside or within the ring and there is calcification below an otherwise normal Bowman's membrane inside the ring (fig 3) The distribution of the clusters does not suggest a nervous or pore distribution Moreover, the preservation of Bowman's membrane inside the ring makes untenable the supposition of Kuan, that the deposits are laid down on the periphery of an altered segment of Bowman's membrane In order to account for the shape of the lesion in accordance with Kuan's view, it becomes necessary to say that the degenerative disease of the nerves involves only the nerves in the periphery of a small circular area, a very unlikely assumption

Saint Luke's Hospital

# INTRANASAL DRAINAGE FOR CURE OF CHRONIC INFECTION OF THE TEAR SAC

INITIAL, TRANSCANALICULAR, INVERTED U-SHAPED INCISION  
TO FACILITATE FULL OPENING OF THE TEAR SAC

DAVID J MORGENSTERN, M D

Assistant Attending in Otolaryngology at the New York Post-Graduate Medical School and Hospital  
BROOKLYN

Chronic tearing of the eye is usually due to blockage of the tear-conducting passages. The cause of the obstruction may be a scar due to injury, chronic inflammation of the mucous membranes leading to stenosis, a foreign body or pressure from a tumor. Most often chronic inflammation of the mucous membranes causes the obstruction, which is usually located at the bottom of the tear sac or in its extension downward into the nasal cavity, namely, the nasolacrimal duct.

Such interference with tear conduction predisposes to chronic infection in the blocked duct. To drain and cure this infection and to restore normal conduction of tears into the nose, a new opening is made above the obstruction through the bone that separates the tear sac from the nasal cavity. In making this opening from the nose to the tear sac, the greatest difficulty, as Bookwalter<sup>1</sup> stated, is encountered in enlarging the opening into the tear sac to the same size as the bony opening. There are two reasons for this. First, the sac is not easily visualized because it is located at the extreme end of the newly formed bony opening, second, the sac recedes from the instrument that attempts to seize it and is pushed farther out of the operator's sight because it is soft tissue, without firm backing for counterpressure when approached intranasally.

As an aid in visualizing the sac and as a means of securing counterpressure, a heavy Bowman probe passed through the canaliculus has been used to push the sac into the newly formed bony opening. This maneuver is of little avail when the sac is small, when it is softened by disease so that the probe perforates it, when a wide space separates the sac from the nasal cavity or when the sac is thickened or tied down by scar tissue. Such unusual scarring and thickening of the tear sac may result from severe inflam-

mation or from laceration, fracture or previous operation in or about this area.

If the sac is thickened or filled with granulations, West<sup>2</sup> advised its intranasal extirpation. To accomplish this, extensive intranasal resection of tissues, namely, submucous resection of the nasal septum, middle turbinectomy and wide resection of the lateral nasal wall, are often necessary.

In this area, so difficult to visualize intranasally, I employ the keener sense of touch to replace vision.<sup>3</sup> By placing the forefinger over the tear sac, one can feel the bony margin surrounding it, as well as an instrument inserted into it, either through the canaliculus or through the nasal cavity. To insert an instrument, a probe, passed through the canaliculus into the tear sac, is first pushed through the bone into the nasal cavity. The end of this probe, projecting into the nose, guides increasingly larger operating hooks, which are slid along it through the bone into the tear sac. With the sense of touch as guide, the tear sac is fully opened. Electrocoagulation is used to destroy the torn portion of the sac and to coagulate the surface of the bony opening. This combats infection and helps prevent closure. This technic is adequate to provide drainage and to effect cure in the usual case of infection of the tear sac, whether purulent or catarrhal.

On the other hand, the opening of a scarred and thickened tear sac has hitherto proved most difficult. I now fully open such tear sacs easily by an added, initial step in technic. During the past year, I had the opportunity of operating in 2 cases of this unusual condition. In each instance the tear sac was so thickened and scarred that I had difficulty in opening it adequately.

2 West, J M Die Technik der Eröffnung des Tränensackes von der Nase aus nach Erfahrung an 130 einschlägigen Operationen, Arch f Laryng u Rhin 27 504, 1913

3 Morgenstern, D J Intranasal Drainage for Cure of Chronic Tear Sac Infection. New Technic Aided by Electrocoagulation So Simplified as to Be an Office Procedure, Arch Ophth 27 733 (April) 1942

Read by invitation before the New York Society for Clinical Ophthalmology, Jan 3, 1944

1 Bookwalter, C F Intranasal Dacryocystostomy, Arch Ophth 49.568, 1920

Mrs R B, aged 67 had a chronic infection of the tear sac of fifteen years' duration with frequent, severe acute exacerbations. I observed her during the last attack, which eventuated in abscess of the sac. After the pus had been evacuated externally and the opening into the sac had healed, I operated and encountered a much enlarged and thickened sac and a hardened lacrimal bone.

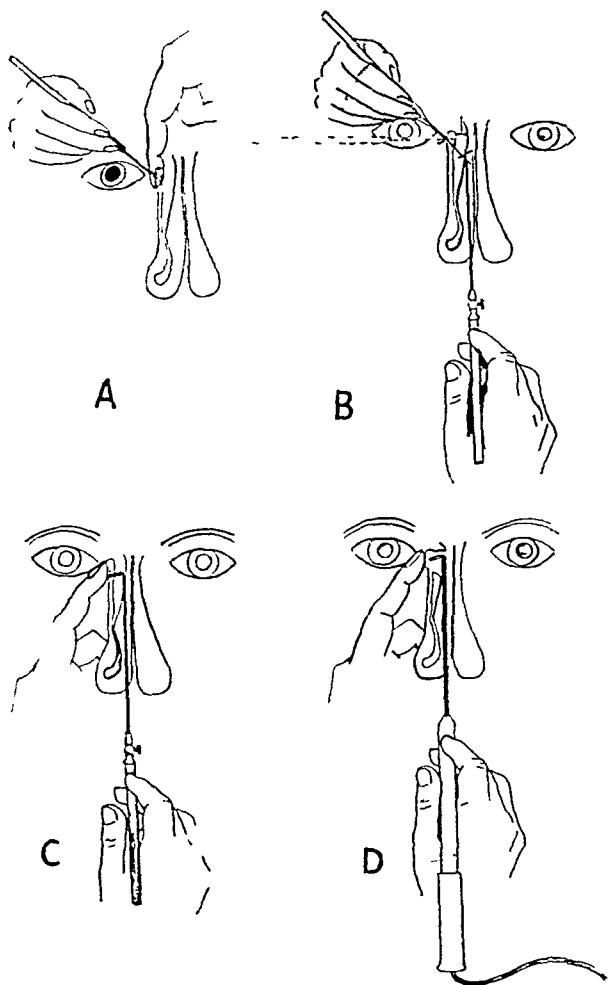
In the second case, that of Mrs G W, aged 54, the left eye had teared for two years. She had been operated on eight months previously by the external dacryocystorhinostomy method of Dupuy-Dutemps and Bourguet. A note from her surgeon stated that because of the thickness and hardness of the bone and the increased width between the nasal cavity and the tear sac he was unable to suture the nasal mucous

the canaliculus to electrocoagulate further the wall of the sac. To give greater counterpressure, against which the point of the sharper instrument could cut through the toughened sac wall, the thumb nail was substituted for the softer palpating forefinger at the inner canthus of the eye. The tactile sensation of the thumb nail is adequate to guide safely the tip of the sharp hooked instrument in opening the sac. To secure greater concentration of the electrocoagulating current, the patient's metal electrode, usually placed in contact with the back, is rolled up and held in the operator's moistened palm, the index finger of which is firmly applied over the tear sac. This more strenuous procedure secured drainage and cure in these 2 cases of chronic infection of the lacrimal sac and restored normal conduction of tears into the nose.

As a result of the experience gained in these, 2 cases, I adopted the additional, initial step in technic to facilitate full opening of the tear sac. I now begin by fully opening the tear sac instead of leaving this most difficult step for the end. This enables me to take advantage of the bony wall of the lacrimal fossa, against which a thin knife, which has been passed through the dilated canaliculus, incises the wall of the sac under the guidance of the palpating forefinger placed over the sac.

The tip of the knife is shifted to the most inferior part of the posterior lacrimal crest. From this point, the knife directed vertically upward and always in firm contact with the bone, an incision is made upward to the top of the fossa along the posterior crest. Here, without its losing contact with the bone, the knife is turned at a right angle, and the top of the sac is cut through. Finally, with the edge of the knife turned downward through another right angle, the wall of the sac is cut downward as far as possible, about 1 mm posterior to the anterior lacrimal crest. To assure complete continuity of the U-shaped incision, I apply electrocoagulating current to the knife, insulated except at its tip, while it incises the wall of the sac. Thus, an inverted U-shaped incision is made in the medial and in part of the posterior wall of the sac. The knife is then withdrawn. Since the top of the sac cannot be palpated, it is better to cut through it at a slightly lower level. Preliminary irrigation of the sac through its being filled, aids in determination of the margins of the sac.

The top and bottom of the knife handle are notched along a line cut by a plane passing through the flat surface of the blade. The fingers feeling these notches correctly direct the knife blade while making the inverted U-shaped incision. The knife edge is so sharpened as to avoid cutting diametrically opposite surfaces of the canaliculus. Slight pressure is exerted on the dull side while the knife is inserted into the canaliculus. Local infiltration of tissues with the anesthetic should not be too great, for it



A, initial transcanicular inverted U-shaped incision to open the tear sac fully. B, small hook on a guiding probe penetrating the lateral nasal wall. C, lateral view of the sac from without, showing the posterior and the anterior (palpated) crest of the fossa sacci lacrimalis and movement of the palpated tip of the hook in the fully opened sac. The hook was the largest used. D, electrocoagulation of sac and fistula, guided by palpation.

membrane to the membrane of the sac through the bony fistula formed. On operating in this case, I encountered hard bone and a greatly thickened and scarred tear sac.

In both cases I used sharper-pointed instruments to tear through and more and stronger electric current to coagulate the wall of the sac. In addition, a Bowman probe insulated except at its tip was passed through

obtunds the sharpness of the lacrimal crests, which are the essential landmarks

From this point, the procedure is practically the same as that described in my original paper.<sup>3</sup> A guiding probe is passed through the lower canaliculus into the bottom of the tear sac and is pushed into the nasal cavity at an angle of about 45 degrees. If several attempts to pass the probe at points posteriorly placed meet with resistance, a few sharp taps on the probe will usually perforate the sclerotic bone.

Examination of the nasal cavity now reveals the end of the guiding probe projecting into it. Four or five hooked instruments are fashioned from various sizes of stiff steel wire, the ends bent at 90 degrees and sharpened. The smallest of the hooks is slid along the back of the guiding probe, penetrating the lateral nasal wall. Palpating with the forefinger of the free hand at the inner canthus, the operator feels for movement of the point of the largest hook, employed last. The guiding probe is now removed.<sup>4</sup> Under guidance of the sense of touch, the bony lacrimal fossa is broken down as widely as possible. This is easily accomplished everywhere except anteriorly, where there is the hard bone of the frontal process of the superior maxilla. A sharp-toothed hook is used to rasp some of this bone. To avoid the strenuous rasping of all this hard bone, the anterior vertical incision through the sac is made about 1 mm posterior to the anterior lacrimal crest. By removal of the bone underlying the medial and part of the posterior wall of the sac and by virtue of the initial, inverted U-shaped incision, a flap is formed. Irrigation with copious amounts of saline solution turns the flap down into the newly formed bony opening into the nose and washes out loose debris.

<sup>4</sup> If the tip of the middle turbinate is enlarged, the obstructing portion is then excised.

Last, to combat closure, as well as to reduce infection, a large, dull-pointed hook, which has been insulated except at its bent end, is used in electrocoagulation of the newly formed opening into the infected tear sac, as well as the sac itself. At the bottom, where the flap has been turned down, the electric current is applied lightly in order to prevent the destruction of the flap. Occasional irrigations of the sac during the healing process maintain the position of the flap in the bony opening and overcome any tendency to stricture which may result from possible injury to the canaliculus. This flap helps to safeguard the permanence of the bottom of the bony opening and aids in epithelization of the bony fistula.

When bone for counterpressure is lacking, only the anterior leg of the inverted U-shaped incision can be made against the hard bone of the frontal process of the superior maxilla. Then the top and the posterior portion of the incision must be attempted with uncertainty. This situation is found in cases in which a previous operation has been performed by whatever method and in which an inadequately opened tear sac has closed while the opening through the bone remains. The same situation exists from time to time when there is a dehiscence or an exceptionally thin lacrimal bone, so that the knife easily perforates it.

One cannot be certain before operation whether the tear sac will prove to be scarred or thickened. Since the inverted U-shaped incision is easily and accurately made as an initial step, and not after the bony backing of the sac has been removed, I have adopted it as the initial step in all cases.

Since there is a minimum of tissue destruction and usually scarcely any bleeding, this procedure can be carried out in the office, the patient being able to leave after a short rest.

433 Eastern Parkway



# BUCCAL MUCOUS MEMBRANE GRAFTS IN TREATMENT OF BURNS OF THE EYE

RALPH SIEGEL, M D

WELCH, W VA

A review of the literature reveals a lack of emphasis on the urgency of immediate transplantation of buccal mucous membrane in the treatment of conjunctival and corneoconjunctival burns. Denig,<sup>1</sup> in 1912, first described the use of mucous membrane in severe lime burns, ammonia burns, and a burn caused by the contents of a golf ball. O'Connor,<sup>2</sup> in a brief review (1933), and Thies,<sup>3</sup> in a German monograph (1938), supported Denig. Von Grolman,<sup>4</sup> in 1940, in South America, reported an isolated case of a labial mucosa graft for a corneoconjunctival burn due to sodium hydroxide. The idea has not received the popularity in this country that it merits, however. Weeks,<sup>5</sup> in 1936, referred to the employment of buccal mucous membrane grafts for trichiasis, symblepharon and trachoma and in treatment of essential shrinkage of the conjunctiva in pemphigus, but he did not mention their use for burns of the eye.

According to Thies, burns of the eye present three stages: first, simple inflammation, in which the subjective complaints are similar to those of traumatic conjunctivitis; second, formation of a profuse exudate; and third, necrosis. Caustic alkalis and certain war gases, notably mustard gas (dichloroethylsulfide) produce corneal damage which, in spite of medical treatment, becomes progressively worse. In cases of such burns the severity of the injury may not be apparent at the time of the accident, but the lesion continues to grow worse. Sollmann<sup>6</sup> pointed out that

From the Department of Ophthalmology, Cook County Hospital

1 Denig, R. *Am J Ophth* **3** 256, 1920, *Circumcorneal Transplantation of Buccal Mucous Membrane as Curative Measure in Diseases of Eye*, *Arch Ophth* **1** 351 (March) 1929.

2 O'Connor, G. B. *Early Grafting in Burns of Eye*, *Arch Ophth* **9** 48 (Jan) 1933.

3 Thies, O. *Die Verätzungen des Auges*, Stuttgart, Ferdinand Enke, 1938.

4 von Grolman, G. *Arch de oftal de Buenos Aires* **15** 429, 1940.

5 Weeks, W. *New York State J Med* **36** 1372, 1936.

6 Sollmann, T. *Manual of Pharmacology*, Philadelphia, W. B. Saunders Company, 1917, pp 125, 131 and 137.

alkalis penetrate the tissues, producing necrosis and soluble albuminates, the action of which continues for several days.

Villard and Delord<sup>7</sup> showed that when sulfuric acid was dropped into the eyes of rabbits the following changes took place: (1) death of the cellular elements of the cornea, with swelling of the corneal lamellae, (2) invasion of the cornea, the anterior chamber and the iris by leukocytes, (3) corneal perforation due to destruction of the cornea by the acid, and (4) cicatrization, in which the corneal opening may be closed by the protruding iris and epithelium from the adjacent conjunctiva.

In severe burns the significant pathologic feature is the necrosis of tissue and the destruction of the perilimbal circulation, including the lymphatics and the marginal plexus formed by the anastomotic arcades of the anterior ciliary arteries. A graft primarily restores the circulation to the limbus and thereby reestablishes the nutrition of the cornea and maintains the normal metabolism. The graft secondarily serves to replace destroyed conjunctiva, with prevention of the sequelae of symblepharon and entropion. Since living conjunctiva is not available in sufficient quantities, the next best substitute is living human tissue similar to conjunctiva itself. Buccal mucous membrane fulfills this crying need and produces practically no abnormal tissue reaction.

Other types of tissue have been used as material for transplantation. Wiener<sup>8</sup> did experimental work on rabbits and monkeys with preserved conjunctival grafts. Conjunctiva was dissected from cows' eyes, stretched over slabs of cork and placed in 4 per cent concentration of solution of formaldehyde U. S. P. Before being used, it was washed with tap water and saline solution. A complete symblepharon was produced in monkeys with concentrated lye, and a conjunctival graft was placed over molding material and secured with lid sutures. The steamy cornea cleared up in about two weeks. In a second monkey a piece of preserved conjunctiva 20 per cent larger than the area of the prepared surface

7 Villard and Delord. *Arch d'opht* **24** 515, 1904.

8 Wiener, M. *J Michigan M Soc* **42** 53, 1943.

was used to cover the defect, and no dental stent was employed. The graft was anchored solely by sutures to the conjunctiva of the host. The healing in this animal was even more rapid than that in the first monkey. The author emphasized that monkeys have more regenerative power than man. Since preservation destroys the life of the cells in the graft, this method depends solely on the ingrowth of cells from the surrounding tissues of the host. Wiener visualized the use of preserved heterogenous grafts in ophthalmic surgery when mucous membrane is needed.

De Rotth<sup>9</sup> recommended the use of fetal membranes in cases of symblepharon when buccal mucous membrane is not obtainable. He used this material in 6 cases of symblepharon and in 2 cases in which the socket had to be enlarged. The fetal membranes were obtained by cesarean section and were kept in tepid Locke's solution from one to fifteen hours. The author admitted that the late results were poor, with nearly total shrinkage of the membrane.

Clay and Baird<sup>10</sup> used grafts from the prepuce and labia minora for the correction of symblepharon and after the removal of large growths from the conjunctiva. These grafts are conspicuous, have a foul odor and desquamate.

Brown<sup>11</sup> advocated the use of a sheet of rabbit peritoneum as a protective covering to separate the cornea and the palpebral conjunctiva until healing is well advanced. The use of rabbit peritoneum as a covering does not stimulate vascularization in cases in which there is impaired perilimbal circulation. Furthermore, it may add insult to injury by exercising a deleterious effect on the cornea.

Zenkina,<sup>12</sup> in the recent Russian literature, tried transplantation of conjunctiva from cadavers for burns of the eye. The conjunctiva was taken from persons who had died of trauma, not later than eighteen hours after death. The material was kept at a temperature of approximately 2 to 4 C in isotonic solution of three chlorides U S P with 2 per cent dextrose for periods ranging from twenty-four hours to four days. Ten cases were reported. The author

concluded that this method offers good results in stimulating the regenerative forces in the surviving tissue and that from the cosmetic angle it is preferable to the autoplasmic buccal mucous membrane graft.

It is my purpose in this paper to call attention by means of case reports to the necessity for the prompt use of buccal mucous membrane in the therapy of conjunctival and corneoconjunctival burns. In this series of 7 cases of ocular burn at the Cook County Hospital, the burn was due to lye (a mixture of sodium hydroxide and sodium carbonate) in 5 cases, to lime (calcium oxide) in 1 case and to gasoline in 1 case. Data on an eighth case of burn due to sulfuric acid were furnished by the late Dr. Sanford R. Gifford and Dr. C. E. Jaeckle, of Chicago. These cases are not only of ophthalmic importance but of forensic interest, since in the 5 cases of burns with lye homicidal intent or intent to disfigure the features of a suitor was involved.

In the order of their severity, the agents causing ocular burns in this series of cases were (1) lye, (2) gasoline, (3) sulfuric acid and (4) lime.

Buccal mucous membrane was obtained with ease and from the patient himself. The wound in the mouth healed promptly and was non-objectionable. There was adequate buccal mucous membrane to supply tissue for the most extensive binocular burn, without too great a sacrifice to the patient's mouth. Except for a secondary buccal hemorrhage in 1 case, which was easily controlled, there were no complications from this angle. Although buccal mucous membrane retained its rosy color and thickness, anatomic and functional restitution was good.

Buccal mucous membrane grafts took in 6 out of 7 eyes which were grafted with this material. The graft sloughed in a case of lye burn of the left eye (case 1) which was so severe and extensive that the entire perilimbal circulation was totally and irreversibly destroyed. In this case the process went on to complete necrosis and corneal perforation in spite of a mucous membrane graft made ten hours after injury. This case indicates that when the circulation has been completely wiped out, there is little hope of salvaging the eye. Later, the subsequent contracted socket was reconstructed by a plastic procedure. The right eye in the same case suffered only a slightly less severe burn. Vision was reduced to counting fingers at 2 feet (60 cm). There was severe necrosis of the palpebral and bulbar conjunctiva, with the typical "porcelain" appearance of the inferior half of the bulb, a sign indicating destruction of the perilimbal circula-

9 de Rotth, A. Plastic Repair of Conjunctival Defects with Fetal Membranes, *Arch. Ophth.* **23** 522 (March) 1940.

10 Clay, G. E., and Baird, J. M. Restoration of Orbit and Repair of Conjunctival Defects with Grafts from Prepuce and Labia Minora, *J. A. M. A.* **107** 1122 (Oct. 3) 1936.

11 Brown, A. L. Lime Burns of Eye. Use of Rabbit Peritoneum to Prevent Severe Delayed Effects, *Arch. Ophth.* **26** 754 (Nov.) 1941.

12 Zenkina, L. V. *Vestnik oftal.* (no. 2) **15** 28, 1939.

tion in this area. A direct burn involved the lower three fourths of the cornea. With prompt grafting a good functional and cosmetic result was obtained. Vision in the right eye returned to 4/10 after three and a half months. The cornea cleared except for a hazy rim at the limbus from 5 30 to 9 30 o'clock, and the cul-de-sac healed, with no sequelae (figure, *A*). Three of the 4 eyes which received buccal mucous membrane grafts not later than ten hours after injury healed with functional and cosmetic results superior to those in eyes which were grafted later than ten hours after the burn.

In this series there were 2 cases of burn due to lye in which grafts were not made. In case 6, that of a bilateral burn with lye with direct corneal involvement and intact perilimbal circulation, equivocal local perilimbal vascular interference appeared in the left eye on the fifth day after the injury. This case occurring early in our experience, a graft was considered unnecessary and the operation was not done. The cornea of the left eye showed delayed progressive corneal infiltration and a corneal ulcer, which appeared three weeks after injury. There was indolent healing, with the development of a large corneal leukoma of the left eye. Vision in the left eye returned to 4/10 only after a long, stormy convalescence.

A lye burn of the left eye, with direct corneal involvement and intact perilimbal circulation, was present in case 7. Since the perilimbal circulation was intact, a mucous membrane graft was not made. A large opaque central opacity developed in the left cornea, with poor functional return. Six weeks after injury vision in the left eye was correctable only to 1/10. It is interesting that infected corneal infiltrates at the periphery appeared ten days after the injury and that a timely delimiting keratotomy, as advised by Dr. Sanford Gifford, probably saved the eye and preserved vision through the superotemporal quadrant of the cornea. It is also noteworthy that in the 2 cases in which grafts were not done what little healing did take place occurred through superficial vascularization in a conjunctival leash that invaded the cornea. These 2 cases indicate that a graft should be made in cases of lye burns in which recovery may occur without a graft, since the eyes with transplanted grafts heal more promptly and with increased vision, less corneal opacity and fewer sequelae.

#### TECHNIC OF GRAFTING

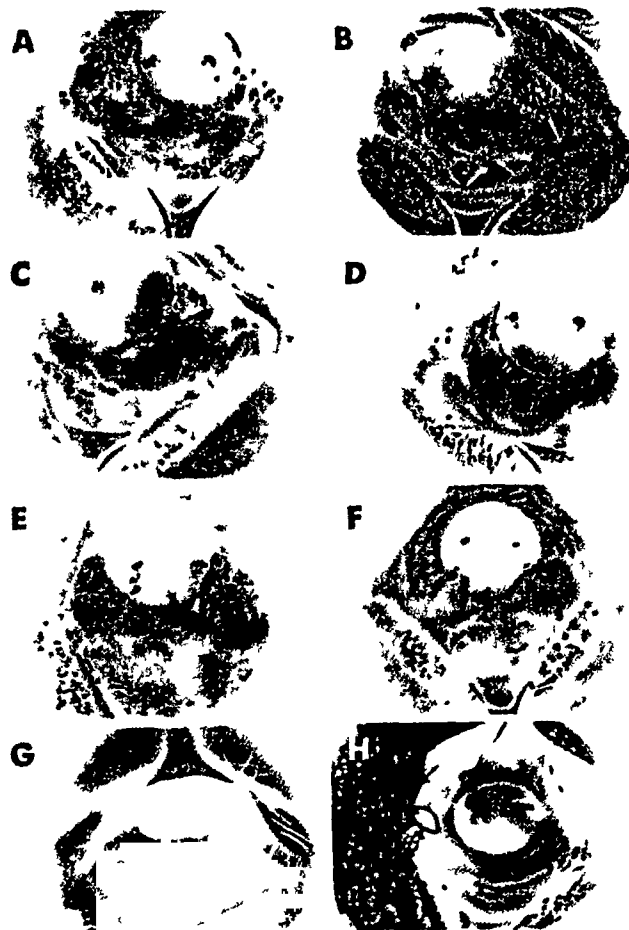
The necrotic conjunctiva and episcleral tissue were excised, and the sclera was scarified with a scalpel. With a large lip clamp and a cataract knife, ample buccal mucous membrane was then taken. The buccal wound

was not sutured. The graft, trimmed of submucous tissue, was applied directly to the denuded area and the margin of the graft sutured by interrupted no. 0025 Deknatel black silk to the intact healthy conjunctiva and the episclera (figure, *B*). When the entire bulbar conjunctiva was burned two horseshoe-shaped circumcorneal grafts were used. Sterile petrolatum was applied in a thin film over the graft. Gauze fluffs were applied under slight pressure and secured with adhesive tape to immobilize, but not to impair, the circulation. Over this dressing was placed a binocular bandage. Secretions were cleansed daily, and an ointment containing 1 per cent atropine was applied. The binocular bandage was removed on the fifth day, and sutures were removed on the seventh day.

#### REPORT OF CASES

CASE 1—H. Y., a Negro aged 39, was admitted on April 28, 1943, several hours after he had been greeted by his "girl friend" with a bucketful of lye thrown into the face and eyes. Vision in the right eye was reduced to counting fingers at 2 feet (60 cm). There was pronounced necrosis of the palpebral and bulbar conjunctivas, with the typical "porcelain" appearance of the inferior half of the bulb, the process extending into the fornix. The lower three fourths of the cornea was dirty gray. Vision in the left eye was reduced to light perception. The entire bulbar conjunctiva was necrosed and dead white, with complete obliteration of blood vessels. The cornea was opaque gray. On April 28, ten hours after the accident, a graft of buccal mucous membrane was made in both eyes. The graft took promptly in the right eye, and on the fifth postoperative day the corneal opacity of that eye appeared to be receding. At the end of two weeks the cornea was clear except for a small, punctate-staining infiltrate at the inferior part of the limbus. The graft of the left eye sloughed completely. There was necrosis of the entire palpebral and bulbar conjunctiva, the cornea and the sclera. This eye, in spite of heroic medical and surgical measures, went on to complete necrosis, with perforation and sloughing of the entire cornea on May 13. The left eye was eviscerated, and the left bulb healed, with adhesions between the scleral stump and the lids, a palpebral fissure slit of 2 cm remaining. Vision in the right eye returned to 4/10 after three and a half months. The entire cornea was clear except for a hazy rim of 3 mm at the limbus from 5 30 to 9 30 o'clock (figure, *A*).

CASE 2—E. T., a Negro aged 20, was admitted on May 12, 1943, one hour after he had sustained burns of the eyes and face with lye as a result of a social accident. Vision in each eye was reduced to counting fingers at 2 feet (60 cm). There were extensive second degree burns of the eyelids and face. The palpebral and bulbar conjunctiva of each eye showed advanced necrosis. The nasal and inferior quadrants of the bulb of the right eye had a porcelain white appearance, with obliteration of the blood vessels, and the nasal and nasal inferior portions of the right cornea were opaque gray as a result of direct burn (figure, *C*). The nasal, temporal and inferior quadrants of the left bulb were porcelain white, and the inferior three fourths of the left cornea was also opaque gray (figure, *D*). Buccal mucous membrane grafts were performed bilaterally nine hours after the injury. On the sixth postoperative day the corneas were clear except for a narrow rim inferiorly. The grafts took, and vision in each eye



*A* (case 1), buccal mucous membrane graft of the right eye three weeks after operation, *B*, buccal mucous membrane graft in place with interrupted black silk, *C* (case 2), lye burn in the right eye one hour after social accident, *D* (case 2), lye burn of the left eye one hour after the accident *E* (case 2), buccal mucous membrane graft of the right eye three weeks after accident, *F* (case 2), buccal mucous membrane graft of the left eye three weeks after accident, *G* (case 5), buccal mucous membrane graft of the right eye two weeks after operation, and *H* (case 8), lye burn of the right eye six hours after the accident



returned to 5/10 after three weeks (figure, *E* and *F*) Selective Service then claimed the patient

CASE 3—H G, a Negro boy aged 7 years, was admitted on May 6, 1943 with an extensive gasoline burn of the left eye and the left side of the face. Vision in the left eye was reduced to perception of hand movements at 2 feet. Vision in the right eye was 20/20. There was a horseshoe-shaped ring of "porcelain" necrosis around the left limbus superiorly. The entire cornea stained deeply with fluorescein. On May 11 a horseshoe-shaped buccal mucous membrane graft was made. On the twelfth postoperative day there was slight clearing of the cornea at the periphery. One month after grafting, vision in the left eye had improved to 1/10. The superior half of the cornea was obscured by a gray opacity, and the lower half of the cornea showed multiple radial striate opacities. The graft was elevated and pink and measured 22 by 9 mm in its greatest diameter.

CASE 4—Data on this case were furnished by Dr. Sanford Gifford and Dr. C. E. Jaecle. L., a white man, was admitted on June 7, 1943, to Passavant Memorial Hospital in the service of Dr. Sanford Gifford for a mucous membrane graft. The patient had suffered a sulfuric acid burn of each eye as the result of a battery explosion one week previously. Vision in the left eye was reduced to 8/40 and that in the right eye to 8/10. The lower half of the left cornea was cloudy, and there was a necrotic, white, avascular area below the limbus. On the fifth day after a buccal mucous membrane graft to the left eye, it was noted that the cornea appeared to be clearing. Two months after the injury the left cornea was entirely clear, and vision in the left eye had returned to 20/25 — 1.

CASE 5—L Z, a white boy aged 9 years, was admitted on Aug. 27, 1942, three days after a playmate threw lime into his right eye. Vision in the right eye was reduced to light perception and projection alone, and that in the left eye, to 1/10. The right cornea was milky gray and stained with fluorescein, and the bulbar conjunctiva from 5 to 8 o'clock was necrotic and porcelain white. The left cornea was clearing with the limbal circulation intact. A buccal mucous membrane graft was made in the right eye on August 29. On the fifth day after operation it was noted that the right cornea was less hazy, with the graft well vascularized. Six weeks after the injury the corneas were clear, and vision was 8/10 in the right eye and 10/10 + 3 in the left eye. The result in the right eye two weeks after operation is shown in *G* of the figure.

CASE 6—J F, a Negro man aged 46, was admitted on Feb. 19, 1943, two hours after his wife threw boiling water and lye into his eyes. Vision was reduced to 3/10 in the right eye and to 1/10 in the left eye. The lower third of the cornea of each eye was gray and opaque, and the perilimbal circulation was intact. On February 24, a rim measuring 2 mm, which appeared chemotic and pale, was noted below the limbus of the left eye from 5 to 8 o'clock. The viability of the circulation was equivocal, the question of a mucous membrane graft was debated, and the operation was not done. The cornea of the right eye responded slowly, but the process in the cornea of the left eye ran a stormy course. On March 3 the lower two thirds of the left cornea showed a deep opacity, and on March 9 a large corneal ulcer, 3.5 by 1.5 mm, developed 3 mm inside the limbus, at 6-30 o'clock. This lesion healed

with a sector-shaped, deep opacification of the cornea involving all layers of the stroma, with folds in Descemet's membrane. On June 1 corrected vision was 5/10 + 1 in the right eye and 4/10 in the left eye. The right eye healed, with a corneal opacity, measuring 3 mm, at 7 o'clock and a nebula which encroached on the center of the cornea.

The left eye finally healed, with a sector-shaped, deep corneal opacity involving the entire inferonasal quadrant of the cornea. A leash of conjunctival vessels at 6 o'clock invaded the cornea for 5 mm, through a superficial conjunctival shelf.

CASE 7—O Z, a Negro aged 41, was referred by the surgical service on May 8, 1943, one day after the left eye, the left side of the chest and the left arm were burned with hot lye thrown by his wife. Vision in the left eye was reduced to perception of hand movements at 2 feet. There was a collar of paleness inferiorly at the limbus, with intact perilimbal vessels, and the left cornea was milky and stained diffusely with fluorescein. Since the perilimbal circulation was intact, a mucous membrane graft was not made. The cornea began to clear peripherally, but infected infiltrates appeared at the edge of the central opacity, and a delimiting keratotomy was performed in the superotemporal quadrant on May 17. With therapy consisting of atropine, mercury bichloride and heat, the corneal lesion responded slowly. On June 12 vision in the left eye was only 1/10 with correction, and a diffuse, opalescent gray opacity involved the entire cornea except for a clear quadrant superotemporally, where a hard, gray, linear scar, measuring 4 mm, separated opaque from clear cornea. At 6-30 o'clock, and converging to a point 2 mm inside the limbus, a wedge of superficial blood vessels invaded the cornea.

CASE 8—W W, a Negro aged 22, was referred by the surgical service on June 21, 1943, for severe burns of the face, eyes and mouth with lye. The patient's wife, six hours previously, had thrown a bucketful of hot lye into his face while he was asleep. The left eye prior to grafting is shown in *H* of the figure. Owing to the extensive burns of the mouth, it was impossible to obtain buccal mucous membrane for grafting. Prepuce grafts to each eye were made six hours after the injury. The left eye, which suffered total destruction of the perilimbal circulation, went on to complete necrosis and corneal perforation. The graft of the right eye took. However, there developed a virulent infection of the face and the right eye with *Bacillus pyocyaneus*, and the graft sloughed in part.

#### COMMENT

Prompt grafting with mucous membrane should be performed in cases of burns of the eye of the following types: (1) direct burn of the cornea with local or complete destruction of the perilimbal circulation, (2) direct burn of the cornea with a perilimbal circulation, the intactness of which is open to question, and (3) burn of the bulb with local destruction of the perilimbal circulation, unaccompanied by corneal involvement.

Early grafting stimulates vascularization, which provides nourishment to the cornea and is responsible for metabolic restoration in the cornea, with early return of functional power. Timely

grafting also prevents formation of scar tissue with symblepharon. If grafting is done too late or is omitted, local anoxemia leads to infiltration of the cornea and leukoma, with sequelae. Necrosis of tissue may give rise to tragic consequences. The observation of a porcelain white sclera offers a grave prognosis unless prompt grafting is performed. Even so, as occurred in 2 cases, the necrosis may be so extensive that grafting is of no avail, and the eye goes on to corneal perforation. Except when the entire perilimbal circulation is totally and irreversibly destroyed, early grafting not only shortens the course of the healing process but offers a better prognosis.

#### CONCLUSIONS

The results, based on 5 cases in which grafts of buccal mucous membrane were made and on 3 cases in which such grafting was not done, indicate the urgency of early grafting in treatment of ocular burns.

Every conjunctival or corneoconjunctival burn of real gravity should have a graft of buccal

mucous membrane as soon as possible after the injury. The criterion for determination of the necessity and urgency of a graft is the destruction of the vascular supply to the cornea.

Buccal mucous membrane is the graft of choice in the treatment of severe ocular burns. Preserved heterogenous conjunctiva and cadaver conjunctiva offer future possibilities but require further clinical trial.

Immediate transplantation of buccal mucous membrane should be done in cases of burns of the eye due to war gases, which cause vascular interference in the perilimbal circulation. The lessons learned in civilian life with buccal mucous membrane grafts may prove of value in prevention of the delayed effects of war gases on the cornea.

The late Dr. Sanford R. Gifford, attending ophthalmologist at Cook County Hospital, made the original suggestion for this work and offered valuable criticism. Dr. Isadore Siegel translated the long German monograph by Thies.

111 Virginia Avenue

# TREATMENT OF METASTATIC MENINGOCOCCIC ENDOPHTHALMITIS

## REPORT OF A CASE

ARLINGTON C KRAUSE, M D, AND WILLIAM ROSENBERG, M D

CHICAGO

Ocular complications of cerebrospinal meningitis are less frequent than they were in years past. Prompt use of meningococcic antitoxin and extensive use of sulfonamide compounds have been responsible for the great reduction in the number of complications. The gravest, most important ocular complication is metastatic endophthalmitis, terminating usually in the formation of an abscess in the vitreous, with subsequent organization, in the formation of a cyclitic membrane and frequently in complete retinal detachment. Endophthalmitis occurs in about 5 per cent of all the cases in epidemics. Lazar<sup>1</sup> cited 30 instances in 575 cases, or 5.2 per cent. Bilateral involvement was present in 9 cases in his series. Lewis<sup>2</sup> reported an incidence of 5.7 per cent in 350 cases, with involvement of both eyes in 4 instances.

Epidemic meningitis is primarily an infection of the blood stream, with localization in the meninges and other organs occurring secondarily. Dunphy<sup>3</sup> stated: "In almost all cases the ocular inflammation begins during the stage of bacteremia or shortly after the meningeal symptoms have made themselves evident. Occasional late involvement of the eyeball occurs, and this is probably due to septic emboli." According to Lewis the earliest occurrence of endophthalmitis was on the second day of the disease and the latest on the twelfth. The average occurrence was on the fifth day. Lazar, in 4 case reports, indicated that involvement of the vitreous was present in all patients on their admission to the hospital. In the first case it was noted twenty-four hours after the onset of the illness and in the second three days afterward, in the third and fourth cases the children were admitted primarily because of the ocular infection. The diagnosis of epidemic meningitis in the latter case was made only after examination of the blood

and the spinal fluid. Meningococci have been cultured from within the eyeball. Pathologic changes in eyes enucleated for meningococcic endophthalmitis include no changes that are pathognomonic and differ in no way from those resulting from endophthalmitis from other sources. Inflammation of the anterior portion of the uvea and the choroid, retinitis, usually with detachment, and abscess of the vitreous with organization are common in almost all cases.

The visual end results of endophthalmitis usually are disastrous. However, Lazar reported 2 cases and Lewis<sup>4</sup> 1 in which complete recovery occurred, with return of normal vision. In Lazar's first case, beginning bilateral endophthalmitis was diagnosed one day after the onset of illness. The anterior chambers and the vitreous were hazy, but apparently no frank abscess or membrane formation was noted. Treatment consisted of intravenous administration of meningococcus antitoxin, and clearing of the eyes was noted in twenty-four hours, with complete recovery in two days. Similarly in the second case bilateral endophthalmitis was diagnosed when the patient was admitted to the hospital three days after the onset. Treatment was instituted immediately with intravenously administered meningococcus antitoxin. In addition, intramuscular injections of milk and subconjunctival injections of mercuric oxycyanide were given. One eye recovered with normal vision; and the other underwent phthisis bulbi.

Lewis reported 1 instance of recovery. In his patient the vitreous was filled with grayish opacities, the iris was not involved and there was no ciliary injection. The opacities absorbed rapidly in one week and completely disappeared. Lewis stated that this condition probably should not be classed as endophthalmitis since apparently only the vitreous was involved. Antimeningococcus serum was given intravenously and intraspinally the day the symptoms first appeared. The injection of antimeningococcus serum or meningococcus antitoxin intraocularly and sub-

From the Division of Ophthalmology, Department of Surgery, the University of Chicago.

1 Lazar, N. K. Early Ocular Complications of Epidemic Meningitis, *Arch Ophth* **16** 847 (Nov.) 1936.

2 Lewis, P. M. Ocular Complications of Meningococcic Meningitis, *Am J Ophth* **23** 617 (June) 1940.

3 Dunphy, E. B. Ocular Complications of Cerebrospinal Meningitis, *Arch Ophth* **15** 118 (Jan.) 1936.

4 Lewis, P. M. Eye Changes in Epidemic Cerebrospinal Meningitis. A Clinical and Pathologic Study of Two Hundred Cases, *Tr Am Ophth Soc* **34** 284, 1936.



conjunctivally has been tried by several observers, with apparently no definite results

The more modern treatment of meningococcic meningitis is with antitoxin given intravenously and sulfonamide compounds administered enterally and parenterally

#### REPORT OF A CASE

Miss J W, aged 18 years, was admitted to Municipal Contagious Disease Hospital on July 11, 1943. At that time she was suffering from meningitis, which had a history of four days' duration. Her temperature was 101.8 F taken rectally, her pulse rate, 120 and her respiratory rate 26. She was irrational. Petechiae were numerous over the body and especially on the extremities. Both eyes were severely injected, and the corneas appeared cloudy. It was difficult to determine whether vision was present. The ocular condition was diagnosed endophthalmitis.

The white cell count of the blood was 59,800, and the red cell count was 3,400,000. No growth was obtained from a blood culture. A lumbar puncture was not made.

Treatment consisted of intravenous administration of 40 cc of antimeningococcus serum in 1,000 cc of 5 per cent dextrose in saline solution within a few hours of the patient's admission to the hospital. This was followed eight hours later by 5 Gm of sodium sulfadiazine given intravenously. Beginning on July 12, at 2:00 a m two more doses of 2 Gm of sodium sulfadiazine were given intravenously four hours apart. After that 1 Gm of sulfadiazine was given orally every four hours until July 23. On July 14 the blood level of sulfadiazine was 19.3 mg per hundred cubic centimeters.

During the first few days the eyes were irrigated with boric acid solution every hour except at night. On July 14 ophthalmic ointment was applied to the eyes. At that time the patient's condition was poor, her temperature was 103 F, her pulse rate 120 and her respiratory rate 24. On this same day the patient complained a great deal of painful joints, which had been tender at the time of admission. She also stated that she was unable to see. On July 15 a solution of 20 per cent mild protein silver was used for eye drops. Two drops of 1 per cent solution of homatropine hydrobromide was used for each eye. On July 16 10 grains of acetylsalicylic acid was given on two occasions. On July 17 a 1 per cent solution of atropine sulfate was instilled in each eye, and this treatment was used periodically during the remainder of the patient's illness. Fifteen grains of sodium salicylate with 5 grains of sodium bicarbonate was given twice daily from July 22 until July 26. Hot compresses were repeatedly applied to the eyes.

By July 25 the patient's temperature had returned to normal, and her general condition was much improved. Her eyes were also less injected than at the time of admission to the hospital, but it seemed doubtful if vision existed.

The patient was released from Municipal Contagious Disease Hospital on July 30, 1943. On that date the temperature was normal, as it had been for five days previously. Although the eyes appeared to be improved, it was difficult to determine whether or not there was

perception of light. There was nothing significant in regard to any of the reports of urinalyses and a final examination of the urine on July 30 revealed normal conditions except for the presence of some albumin.

On July 30, 1943 she was admitted to the medical isolation service of Dr C Phillip Miller at the Albert Meritt Billings Hospital, the University of Chicago. Treatment was begun with 3 Gm of sulfadiazine, followed by 1 Gm every four hours. Examination of the eyes at that time revealed vision in each eye reduced to perception of hand movements at about 3 feet (90 cm), and also intense bilateral photophobia, severe mixed bulbar injection and extreme ciliary tenderness. The corneas and the anterior chambers were extremely hazy and the pupils were irregularly dilated and adherent to the lenses. A yellow dense exudate was seen behind each lens, so that details of the fundi could not be seen. Markings on the irises were obliterated, and dull red reflexes were obtained from the pupillary spaces on transillumination. The diagnosis was metastatic meningococcic endophthalmitis of the right and the left eye. Instillation of 1 per cent solution of atropine sulfate three times a day in each eye and typhoid fever therapy were begun. Although no blood cultures were obtained at Municipal Contagious Disease Hospital, on July 3, 1943 the patient's blood serum agglutinated type I meningococci in titers of 1:32. There was no agglutination with type II or type IIa. It was presumed that the infection must have been with type I.

After consultation with Dr Miller it was decided to treat the patient with penicillin administered by iontophoresis. The penicillin was produced by E R Squibbs & Sons (25,000 Florey units per ampule) and was supplied<sup>5</sup> by the Committee on Medical Research of the Office of Scientific Research and Development by arrangement with Dr Chester S Keefer. The solution was made up in 0.9 per cent solution of sodium chloride so as to contain 1,000 units per cubic centimeter.

Two drops of a solution of penicillin containing 1,000 Florey units per cubic centimeter was instilled into the conjunctival sacs. The lids were closed and negative electrodes placed over the closed lids with a positive electrode placed over the neck. Two milliamperes of current was allowed to pass for five minutes in each eye. This procedure was repeated on July 31 and Aug 1. From August 2 to August 24 a current of 3 to 4 milliamperes was allowed to pass for ten minutes in each eye. She received typhoid fever therapy on July 31 and on August 14, the reaction was a moderate fever. In addition, the sulfadiazine therapy was continued until Aug 4.

Examination of her eyes was extremely difficult, because of excessive photophobia and poor cooperation. The fundi were examined with the patient under methylene anesthesia, on August 9, 16 and 26. On August 9 both eyes showed a severe anterior uveal reaction with distinct conjunctival injection. The corneas were extremely hazy, the anterior chambers were cloudy, there were complete posterior synechia, as before, early seclusio and occlusio pupillae, pro-

<sup>5</sup> The penicillin was provided by the Office of Scientific Research and Development from supplies assigned by the Committee on Medical Research for clinical investigations recommended by the Committee on Chemotherapeutic and Other Agents of the National Research Council.

nounced atrophy of the irises and proliferation of pigment. The right fundus showed a red, granular reflex uniformly. A small white cloud was present over the disk. The vitreous was extremely hazy, and no details could be seen. The left fundus showed a yellow reflex, with a questionable suggestion of a pink reflex below. On August 16 the media of the right eye showed some clearing, so that the retinal vessels could be recognized faintly. The left eye still showed no red reflex. The external reaction continued to be severe in both eyes. On August 26 there was no change in the left eye, but the right eye began to show evidences of clearing, externally and internally. The bulbar reaction was less intense, and the retina showed more clearly. A light white haze was seen on the disk between 3 and 6 o'clock and on the adjacent retina about  $\frac{1}{2}$  papilla diameter from the area. The macula was seen, but no foveolar reflex could be made out.

The patient was discharged from the hospital on September 2. She was seen in the outpatient ophthalmic clinic on September 18. Her mother stated that gradual improvement had occurred while she was at home, so that the patient's eyes had gradually become white and she had begun to open them spontaneously. Photophobia had almost completely disappeared, she walked around the house unaided and was able to perform simple tasks with ease, such as washing dishes. Vision in the right eye was 20/200 as determined by the Snellen chart, and she could distinguish hand movements with the left eye. It was believed that she could probably see more than the chart indicated.

On October 29 the patient was seen again in the outpatient clinic. The mother reported that she had improved remarkably well, so that she could carry on all of her normal activities. There was no voluntary or involuntary blepharospasm, the eyes remained completely white and there was no indication of any discomfort. Vision in the right eye was 20/50 + 2 as measured on the Snellen chart and 20/30 when tested with the number chart. She could only distinguish hand movements with the left eye. The right eye was white, there was no evidence of any active inflammation, the pupil was irregularly dilated and completely adherent to the lens. The cornea was clear. The tactile tension was normal. Slit lamp examination of the anterior segments was not possible because of poor cooperation, although examination with the ophthalmoscope revealed no gross lesions of the retina. The disk and the vessels appeared normal, and the macular area, although not well seen, also looked normal. There was a slight generalized haze of the vitreous, but no discrete opacities were seen. The left eye revealed a clear cornea and a large, irregularly dilated pupil, completely adherent to the lens. A dense white opaque mass occluded the pupillary space. The tactile tension was slightly less than that of the right eye.

#### COMMENT

The patient on discharge from the hospital after treatment for meningococcic infection had bilateral metastatic endophthalmitis, leading apparently to total blindness. She was again admitted to the hospital for treatment with penicillin. Penicillin was chosen because it is bactericidal

and bacteriostatic and is superior to the sulfonamide drugs in that its activity is not inhibited by large numbers of bacteria or by the presence of pus or autolysates of tissue. Furthermore, treatment with sulfadiazine caused no evident improvement of the ocular disease. No report on the use of penicillin for clinical meningococcic infection was found in the literature. However, Hobby, Meyer and Chaffee<sup>6</sup> found that meningococci were susceptible in vitro to the bactericidal or bacteriostatic action of penicillin.

The choice method of administration of penicillin is intravenous or intramuscular injections for generalized infections and local applications for focal infections.<sup>7</sup> Frequent small doses are better than less frequent larger doses, since the tissues require a constant concentration. Treatment is continued until clinical signs have disappeared.<sup>8</sup>

Because of the small quantity of penicillin which was available and because of the localization of residual meningococcic infection a decision was made to try iontophoresis. Recently Boyd,<sup>9</sup> using sodium sulfathiazole, and von Sallmann,<sup>10</sup> using scopolamine hydrobromide and atropine sulfate, found that a decided increase in the concentration of the drugs in the cornea and the aqueous humor may be obtained by means of iontophoresis. Von Sallmann<sup>11</sup> later made similar observations after trying sulfadiazine and penicillin on experimental animals.

In those cases in the literature in which recoveries were reported ocular complications were present and diagnosed early, i.e. within the first five days, and treatment was begun immediately. Cure was attributed to the specific general and not local therapy. There were no instances of recovery after the pathologic process seemed to be well established. Indeed treatment was not directed specially to the ocular complications, but these responded to treatment of the

6 Hobby, G. L., Meyer, K., and Chaffee, E. Activity of Penicillin in Vitro, *Proc. Soc. Exper. Biol. & Med.* **50** 277 (June) 1942.

7 Rammelkamp, C. H., and Keefer, C. S. The Absorption, Excretion and Distribution of Penicillin, *J. Clin. Investigation* **22** 425 (May) 1943.

8 Florey, M. E., and Florey, H. W. General and Local Administration of Penicillin, *Lancet* **1** 387 (March 27) 1943.

9 Boyd, J. L. Sodium Sulfathiazole Iontophoresis, *Arch. Ophth.* **28** 205 (Aug.) 1942.

10 von Sallmann, L. Iontophoretic Introduction of Atropine and Scopolamine into the Rabbit Eye, *Arch. Ophth.* **29** 711 (May) 1943.

11 von Sallmann, L. Penicillin and Sulfadiazine in the Treatment of Experimental Intraocular Infection with *Pneumococcus*, *Arch. Ophth.* **30** 426 (Oct) 1943.

meningococcemia as a whole. The clinical application of iontophoresis of penicillin as a means of attaining a more rapid and concentrated penetration of the drug in the eye, as presented in this case is evidently well worth a trial.

#### SUMMARY

The treatment of metastatic meningococcic endophthalmitis after recovery of the patient from meningitis has been considered hopeless. A patient with meningococcic endophthalmitis was

treated with sulfadiazine given by mouth and penicillin applied by ocular iontophoresis. There is reason to believe that penicillin and sulfadiazine were the effective agents producing recovery from unilateral endophthalmitis in our patient. Recovery was remarkable in that the disease process was present without remission for twenty-four days before treatment was begun. There was no response to the usual therapeutic methods, and favorable prognosis appeared hopeless.

# STRABISMUS IN ADULTS

## ANALYSIS OF OPERATIVE RESULTS IN SIXTY-FIVE CASES

MAJOR IRVING I SHURE

MEDICAL CORPS, ARMY OF THE UNITED STATES

The importance of proper treatment for strabismus has been emphasized by Peter,<sup>1</sup> Wilkinson<sup>2</sup> and Davis<sup>3</sup>. A review of the recent literature on strabismus shows that inadequate emphasis is placed on the necessity for proper treatment of adults so affected. The feeling of inferiority among these patients is inconceivable. One cannot appreciate the timidity, the lack of initiative and the complete introversion of these otherwise intelligent people unless one has had the opportunity of treating a large number. I report here an analysis of results in 65 cases of strabismus in adults, all of whom underwent operative procedures and received orthoptic treatment. The results obtained in this series, from the standpoint both of the cosmetic effect and of functional recovery, convince me that too many ophthalmologists have developed an attitude of defeatism toward the treatment of this condition. Much can be accomplished for patients with this disorder, and it is hoped that this analysis will lead others to pursue a more aggressive course of treatment.

A proper diagnosis of the type of strabismus present is equally as important in adults as in children. Before treatment is instituted in any case, the following procedures should be carried out: (1) a complete history, including date of onset and the presence of a familial tendency, should be obtained, (2) refraction should be done, (3) the amount of deviation should be estimated, (4) the near point of convergence should be determined, (5) the degree of fusion, if any, should be measured, and (6) the presence or absence of anomalous retinal correspondence should be noted. This routine was followed in the series of cases studied.

1 Peter, L. C. *Technic of Orthoptic Training in Squint*, Arch Ophth **14** 975-984 (Dec) 1935

2 Wilkinson, O. *Early Treatment of Squint*, South M J **34** 844-846 (Aug) 1941

3 Davis, W. T. *Ocular Motility Then and Now*, South M J **36** 228-234 (March) 1943

4 Lordan, J. P. *Orthoptic and Surgical Management of Strabismus*, Arch Ophth **12** 843-849 (Dec) 1934

5 Guibor, G. P. *Early Diagnosis and Non-Surgical Treatment of Strabismus*, Am J Dis Child **52** 907-915 (Oct) 1936

An accurate history is essential, and its importance has been stressed by Lordan<sup>4</sup> and Guibor<sup>5</sup>. The age at onset and the presence or absence of a hereditary tendency are of the utmost importance in arriving at a proper diagnosis. The appearance of a strabismus soon after birth, or at 6 months of age, indicates a nonaccommodative type. Visual acuity is usually 20/20 in both eyes. Complete absence of the fusion faculty was demonstrated in patients with strabismus by Peter<sup>6</sup> and Worth<sup>7</sup>. Burri<sup>8</sup> did not admit the presence of a specific fusion center but expressed the belief that fusion is an act of learning, comparable to that of walking or talking. I am in agreement with Peter and Worth with respect to the presence of a fusion center and am convinced of its importance in the causation of strabismus. The absence of a fusion faculty predicates a poor prognosis. But if fusion is present in any degree, it can be developed in persons well past middle adult life (Peter<sup>6</sup>).

Refraction should be done under full cycloplegia. All patients in this series were examined under cycloplegia induced with 1 per cent homatropine hydrobromide, several drops being administered every ten minutes for six doses. The degree of strabismus was noted and recorded before and during the cycloplegia. Postcycloplegic examination was performed ten days later. Fundoscopic examination revealed the presence of any ocular disease.

The degree of deviation was estimated by two methods. When practical, the screen test was utilized, and the movements of both eyes were neutralized by means of prisms. A state of suppression, amblyopia or poor fixation is common in adult patients with strabismus. Davis and Sheppard<sup>9</sup> have shown that the screen and prism test is useless with such patients and that one

6 Peter, L. C. *Extra-Ocular Muscles*, ed 3, Philadelphia, Lea & Febiger, 1941, pp 216-218

7 Worth, C. *Squint*, ed 5, Philadelphia, P. Blakiston's Son & Co., 1921, p 78

8 Burri, C. *Process of Learning Simultaneous Binocular Vision*, Arch Ophth **28** 235-244 (Aug) 1942

9 Davis, W. T., and Sheppard, E. *Interpretation and Evaluation of Tests for Strabismus*, South M J **34** 559-565 (June) 1941

must resort to the perimeter. This instrument was used in every case in this series, usually in addition to other means of strabismometry. The strabismus was measured for 20 feet (6 meters) and for 13 inches (33 cm).

The importance of a proper evaluation of the existing status of the near point for convergence in patients with strabismus was stressed by Jameson<sup>10</sup>. He maintained that the condition of the



Fig 1—A, divergent strabismus in the right eye, with a deviation of 35 degrees. Visual acuity was 20/20 in both eyes. B, result obtained by recession and advancement of the internal rectus muscle and recession of the external rectus muscle. Fusion grade 3 was obtained.

musculature, or, rather, its innervational status, can be determined by this procedure. White<sup>11</sup> placed great importance on determination of the deviation for 20 feet and for 13 inches. If the case is one of convergent strabismus and the deviation is greater for distance than near vision, the condition is recorded as divergence insufficiency. If the deviation is greater for near vision, convergence excess is present. In the case of divergent strabismus, if the deviation is greater for distant than for near vision, divergence excess is present, and if the deviation is greater for near vision, convergence insufficiency exists. Wilkinson<sup>12</sup> divided convergent strabismus into the static and the dynamic type. Static convergence is equal to the squint. The patient fixes an object with his straight eye. The object is gradually brought toward the eye, and the movements of the deviating eye are

noted. The point at which the deviating eye corrects itself is the near point. If, when the object is brought closer to the eye, the convergence is increased, an excessive dynamic convergence, or convergence excess, is indicated. If the eyes tend to correct themselves without further convergence, a divergence insufficiency exists. A study of the results obtained in the present series of cases by these methods shows that the two procedures arrive at the same conclusion in somewhat different ways. The type and extent of the operative procedure to be employed can be determined by the results obtained from these tests.

The ultimate aim in any method of treatment for strabismus is ability to obtain and maintain stereopsis. Feldman and Taylor<sup>13</sup> noted three grades of binocular vision: (1) binocular macular perception, (2) superimposition of images and (3) stereopsis. Burian<sup>14</sup> defined binocular macular perception as the visual state in which both retinas are stimulated simultaneously at points having the same innate, or common, visual direction. The two images falling on the two foveas are then converted into one image, thus, only one object is seen. This superimposition, or the combining of two images into one, is known as fusion, or the second stage. Fusion precludes the presence of a properly functioning fusion faculty. Determination of the presence and degree of fusion is most important in all



Fig 2—Alternating strabismus, with a deviation of 43 degrees. Visual acuity was 20/20 in both eyes. B, result of resection and advancement of the internal rectus muscle and recession of the external rectus muscle of both eyes. Fusion grade 3 was obtained.

10 Jameson, P. C. Entity of Muscle Recession, *Arch Ophthalm* **21** 362-370 (Feb) 1939.

11 White, J. W. The Importance of a Complete Diagnosis to a Successful Treatment of Strabismus, *Surg Gynec & Obst* **74** 565-566 (Feb) 1942.

12 Wilkinson, O. Strabismus: Its Etiology and Treatment, ed 1, St. Louis, C. V. Mosby Company, 1927, pp 135-136.

cases of strabismus, both from a prognostic and from a therapeutic standpoint. A stereoscope of

13 Feldman, J. B., and Taylor, A. F. Obstacles to Squint Training—Amblyopia, *Arch Ophthalm* **27** 851-868 (May) 1942.

14 Burian, H. M. Fusional Movements in Permanent Strabismus, *Arch Ophthalm* **26** 626-652 (Oct) 1941.

standard make, with use of the cards devised by Wells, affords an ideal and inexpensive instrument for the measurement of fusion. This instrument was used in all cases reported in this series.

The presence or absence of anomalous retinal correspondence was determined in each case by means of the after-image test, as advocated by Bielschowsky.<sup>15</sup>



Fig 3—A, convergent concomitant strabismus in the left eye, with a deviation of 18 degrees. Visual acuity was 20/20 in the right eye and 20/100 in the left eye. B, result obtained by resection of the external rectus muscle and recession of the internal rectus muscle. No fusion or improvement of vision resulted.

#### ANALYSIS OF CASES

A total of 65 operative cases is reported in this study. All the patients were men, in good health. A review of the observations reveals the following interesting facts:

**Age**—The youngest patient operated on was 18 years of age, and the oldest, 39. The average age for the entire series was 27 years.

**Degree of Deviation**—As stated in the first part of this paper, I found the perimeter an excellent instrument for measuring the amount of deviation. In the 51 cases of convergent strabismus the lowest amount of deviation was 8 degrees, and the highest, 45 degrees. In 2 cases between 5 and 10 degrees, in 12 cases between 1 and 20 degrees, in 23 cases between 20 and 30 degrees and in 4 cases over 40 degrees of deviation was present. Analysis of the cases of divergent strabismus showed deviations of between 20 and 30 degrees in 6 cases and of between 30 and 40 degrees in 6 cases. The left eye was the squinting eye in 25 of the cases of convergent strabismus, and the right eye was the offender in the remaining 26 cases. Analysis of the cases of divergent strabismus showed that

the squint was in the left eye in 5 cases and in the right eye in 7 cases.

**Refractive Error**—In practically all cases in this series refraction had been carried out at various times, and refractive errors had been prescribed for prior to examination at the station hospital. In all patients, however, recent the last refraction, examination was again made under full cycloplegia. Of the 65 cases studied, no refractive error was present in 31. Interestingly, into the latter group fell a number of cases with deviations of 40 degrees or over. No definite relation could be shown between the degree of deviation and the refractive error, an observation corroborating that of Dunnington and Wheeler.<sup>16</sup> In 2 cases there were refractive errors of over 3 D. In 4 cases of convergent strabismus there was minimal myopia. In 5 cases of convergent strabismus the squint was of the accommodative type. In the last-mentioned cases the wearing of the corrective lenses reduced the amount of deviation from 4 to 20 degrees.

**Amblyopia and Visual Acuity**—Amblyopia was taken to mean the missing of the first three lines on a standard Snellen chart or vision below 20/50. Cases were eliminated in which the fundus was pathologic. There were 12 cases



Fig 4—Convergent concomitant strabismus, with deviation of 28 degrees in the right eye. Visual acuity was 20/40 in the right eye and 20/20 in the left eye. B, result of resection and advancement of the external rectus muscle and recession of the internal rectus muscle. Fusion grade 2 was obtained.

of amblyopia, in 7 of which refractive errors above 2.5 D were present. In the remaining 3 cases no refractive error was noted. This

<sup>15</sup> Bielschowsky, A. Lecture on Motor Anomalies. IV. Etiology of Strabismus, *Am J Ophth* 21:329-342 (Dec) 1938.

<sup>16</sup> Dunnington, J. H., and Wheeler, M. C. Operative Results in Two Hundred and Eleven Cases of Convergent Strabismus, *Arch Ophth* 28:1-11 (July) 1942.

indicates a definite relation between refractive error and amblyopia, probably through suppression of the squinting eye

*Type of Operation*—The type of operation to be performed in each case was determined only after a review of the clinical data. If hyperirritability of the internal rectus muscle was present, i. e., convergence excess, a maximum recession was performed on that muscle. If, on the other hand, divergence insufficiency prevailed, the maximum operative effort was expended on a resection and advancement procedure of the external rectus muscle. More satisfactory results were obtained in cases in which a recession of one muscle was combined with a resection and advancement of the opposing muscle. I am in complete agreement with Jameson,<sup>10</sup> who stated that the internal rectus muscle is much more sensitive to recession than the external rectus muscle and that measured recessions are quite satisfactory. After a thorough trial, it was found that for each millimeter of recession or resection of the internal rectus muscle, approximately 3 degrees of deviation will be corrected. Likewise, each millimeter of operative effort on the external rectus muscle will yield about half this correction, or 1.5 degrees. If these figures are used as a guide in calculating the approximate procedure on each muscle prior to operation, a most satisfactory cosmetic result will obtain in the majority of cases. This statement is made with full realization of the individual variations and anatomic differences that an operator invariably encounters.

#### TECHNIC

The method of tendon recession described by Jameson<sup>10</sup> and Wiener and Alvis,<sup>17</sup> with slight modification, was employed. A vertical incision is made over the insertion of the tendon of the muscle to be operated on. Good exposure is obtained by blunt dissection for a distance approximately equivalent to the diameter of the cornea. The capsule of Tenon is grasped below the tendon's lower border and carefully snipped, and the point of a tendon hook is introduced beneath the muscle. Care is taken to include all the muscle fibers on the hook. The point is then allowed to show through the opposite border by rotation of the hook toward the operator, and Tenon's capsule is again snipped. A second tendon hook is placed in the last opening made, and the fibers of the capsule of Tenon, the ligament of Lockwood and adjacent structures are all carefully dissected free. The bluish white sclera can be seen beneath. Two double-armed sutures of no. 0000 plain catgut, threaded in atraumatic needles, are used. The sutures are passed through the tendon from the scleral surface upward, one suture on each end, and placed as close to the scleral attachment as possible. The muscle

is then severed from the sclera. The amount of recession having been previously computed, a point marking the new site of insertion on the sclera is made. The atraumatic needles are carefully teased through the superficial fibers of the sclera, on as broad a base as the area of original insertion. The sutures are then securely tied, and the conjunctiva is closed with an uninterrupted black silk suture. In the procedure of resection and advancement, the conjunctiva is opened and the muscle exposed in a manner similar to that for recession. A vertical incision is made over the tendon of the muscle involved, approximately 7 mm back of the limbal margin, and the incision extended the length of the cornea. Tenon's capsule is carefully picked up at its lower border and snipped. The point of a tendon hook is introduced into the opening and carried beneath the muscle, care being taken to include all the muscle fibers. The hook is then brought against Tenon's capsule, which is snipped at its upper border, and a second tendon hook is placed into the latter opening. All fibers of Tenon's capsule are then carefully dissected free, and the entire muscle is exposed toward the equator of the globe by separating the two hooks. Two double-armed, atraumatic sutures of plain no. 0000 catgut are used. The amount of muscle to be resected or advanced having been carefully calculated by the micrometer, one of the double-armed sutures is inserted at the measured point into approximately the central portion of the muscle. The second needle of the same suture is then similarly placed near its lateral border. The latter suture is once more brought around the lateral margin of the muscle for additional fixation. The second suture needle is similarly brought through the opposite border of the muscle, as described. A firm grasp is taken on both sutures, which are held upward, and the muscle is severed. The excess muscle at the stump is cleanly removed down to the sclera. With firm fixation at the stump by means of forceps, the muscle is reinserted into the new point by carefully teasing the needle through the superficial layers of the sclera. Since the conjunctiva is firmly adherent at this point, it is well to see that clean dissection has been performed. Care must be taken to see that a firm bite is taken into the scleral fibers in this region. The muscle is carefully brought up to its new insertion and tied. A single running black silk suture is used to close the conjunctiva. Only the eye operated on is bandaged, the good eye being left open. The bandage is removed in twenty-four hours, and the usual post-operative chemosis is controlled with cold packs. The patient is placed under orthoptic training forty-eight hours after operation. Sessions begin with fifteen minute periods twice daily and are gradually increased to thirty minutes twice a day. The sutures are removed from the conjunctiva on the fifth day, and the patient is discharged to duty in ten days.

As previously stated, a surprisingly accurate estimate of the amount of muscle to be recessed, resected or advanced can be made in a large number of cases. The amount was based on the principle of a 3 degree correction for each millimeter of recession of the internal rectus muscle and a 1.5 degree correction for each millimeter of recession of the external rectus muscle. An ordinary micrometer was used at the operating table to determine the amount of the operative procedure. It will be found that observation of the general rule just stated will result in approximate parallelism of the eyes in a great majority of cases, especially if

17 Wiener, M., and Alvis, B. *Surgery of the Eye*, ed 1, Philadelphia, W. B. Saunders Company, 1940, pp 355-356



careful study has been given to the status of the muscle primarily involved

Elimination of the Prince or Noyes muscle forceps has been achieved merely by substitution of sutures to fix the muscle. Use of the latter allows a clearer field, with better exposure of the operative site. Crushing of the muscle is also avoided.

The statement of Jameson<sup>10</sup> that "it is better to leave a slight convergence than to run the risk of an over-correction," has not received confirmation from the results in this series. I have consistently found that patients with parallelism on leaving the table will show residual convergence when examined several months later. If, on the other hand, about 5 degrees of divergence is present at the time the operation is finished and the patient is placed under supervised orthoptic training within forty-eight hours, not only excellent cosmetic results but various degrees of fusion will be obtained in a great number of cases. It is granted that the results obtained in the treatment of strabismus are extremely variable. In the majority of cases, however, results are satisfactory if fundamental principles are adhered to, evaluation of muscle power is properly performed and good surgical technic is employed.

The older method of bandaging both eyes for four to five days after an operation on the ocular muscles has been found necessary. It is now known that the eyes assume not only the position of rest beneath bandages, i. e., up and out, but that considerable movement takes

An attempt was made, through careful individualization, to ascertain the type of operation most suited in the particular case. The 65 cases were broken down into four groups on the basis of the operative procedure. In 55 cases a recession combined with a resection and advancement of the opposing muscle was done. A shortening operation of one muscle only was performed in 2 cases while a recession of one muscle and a resection of the opposing muscle, with reinsertion at its original site, were performed in 2 cases. In the remaining 6 cases resection and advancement were performed on one muscle, with no operation on its antagonist.

In 14 of the 55 cases in which recession was combined with resection and advancement, under-correction resulted. In 7 of these cases a second operation was required, and in 1 case four operative procedures were necessary. In the remaining 6 cases there was no further operative intervention, for one reason or another. Satisfactory parallelism of the eyes was obtained in all 7 cases in which the second operation was performed. It is significant that, though the

#### *Analysis of Results of Operative Treatment in Fifty-One Cases of Strabismus in Adults*

Type of Strabismus	Number of Cases	Over-correction	Under-correction	Second Operative Procedure	Fusion Final Result			
					None	Grade I	Grade II	Grade III
Convergent	51	0	12	5	25	5	7	14
Divergent	12	0	2	2	3	1	3	5
Alternating	2	0	0	0	0	1	0	1

place. Only the eye operated on was bandaged after each operation, and the bandage was removed in twenty-four hours. If care is taken at the time of operation to see that a good bite is taken into the scleral fibers, slipping of the suture need not be feared.

#### RESULTS

Two methods of analysis lie open in any review of strabismus treated by operation. Many surgeons are content to achieve a satisfactory cosmetic result. The value of such an achievement to the patient's psychologic makeup is unquestioned. Only the surgeon who has seen children, and even adults, made introverts by pronounced strabismus can appreciate the joy which the patient will express over a result that he often questions. The second objective, and certainly the one all surgeons treating abnormalities of the ocular muscles should strive for, is that of fusion and stereopsis. In each case in this series the patient's ability to attain fusion was evaluated prior to operation. In cases of amblyopia of course this possibility becomes remote. A good cosmetic result must, of necessity, suffice in a case of the latter defect.

methods of measurement of the squint and the operative figures remained the same, the cases in which there was a small primary deviation were the cases in which an undercorrection resulted.

An interesting fact revealed in this study concerns the behavior of divergent strabismus. In 12 cases of this type of squint recession combined with resection and advancement was employed. In no case did overcorrection result. The cosmetic results were excellent, although the deviations were by far the most extreme of those in the entire series. In the 2 cases in which recession of one muscle was combined with resection of the opposing muscle, deviations of 15 and 16 degrees were noted. Final results showed cure in both cases. Resection of one muscle resulted in production of a cure in the 2 cases in which this method was employed. The deviations were 8 and 15 degrees respectively. In all 6 cases in which resection and advancement of one muscle only were done deviations ranged from 8 to 18 degrees. A good cosmetic effect was obtained in all cases.



No patient in the entire series was considered cured until a thorough trial was made to develop fusion. An ordinary stereoscope was used, consisting of two lenses of + 5.25 D each, separated by a distance of 8.5 cm. The method of the preliminary test advocated by Linksz<sup>18</sup> was used. It was found that the charts devised by Dr Wells gave the best results in the development of fusion. Each patient was given orthoptic training on removal of the bandage, usually about forty-eight hours after the operation. Treatments consisted of two sessions of fifteen minutes each day for one week, after which the treatment periods were lengthened to thirty minutes. All exercises were supervised, and a daily record of the patient's progress was carefully noted.

The basis for the orthoptic procedure lies in the brain's abhorrence of diplopia produced by the stereoscope. As the patient looks into the instrument, the images tend to move together, since this is the only method by which the diplopia can be overcome. Because both macules are stimulated simultaneously, suppression of either image is virtually impossible. This presupposes, of course, the presence of binocular macular perception.

It has long been recognized that the presence of suppression, amblyopia, poor fixation or anomalous retinal correspondence constitutes obstacles in the development of fusion. An attempt was made in each case to break down the influence of these factors by means of flash illumination, mental reeducation and daily treatments with the stereoscope. Often two or more of these conditions were present in 1 case. In some cases an obstacle of this kind proved refractory to all orthoptic training, and my associates and I were content to call a good cosmetic result a cure in several instances of this type.

A review of the results obtained with orthoptic training after operation was most gratifying. An average of twenty treatments was given each patient in this series. The smallest number of treatments given to one patient was twelve, the largest, thirty-two. These treatments were all given at daily intervals. The results were recorded as no fusion, fusion grade 1 (simultaneous binocular macular perception), fusion grade 2 (superimposition of images) and fusion grade 3 (stereopsis). In 28 cases no fusion developed after prolonged orthoptic training. Fusion grade 1 was obtained in 7 cases, fusion grade 2 in 19 cases and fusion grade 3 in 20 cases. When it is remembered that amblyopia was present at the start of the treatments in 12 cases, it can

readily be seen that the results obtained were surprisingly good.

#### COMPLICATIONS

In no case in the entire series did postoperative infection result. The usual chemosis following operative trauma was easily controlled with cold compresses. In 3 cases granulomas of the conjunctiva occurred, the result of imperfect closure of the conjunctiva at the time of the operation; they were removed later. Considerable thickening and swelling often persisted at the operative site for several months. This condition was due to slow absorption of the catgut. No disability or deformity resulted, and in all cases clearing was uneventful.

Transient diplopia was present in fully 75 per cent of cases immediately after operation. In some cases this persisted for two or three days, with gradual merging of the two images and disappearance of symptoms. In 6 cases annoying diplopia of various degrees was encountered. In 3 of these cases the diplopia proved amenable to orthoptic training, with final complete cure. In 2 of the remaining 3 cases some annoyance continued. In these cases the condition gradually improved under intensive orthoptic training, although the response to treatment was slow. In 1 case, however, the diplopia proved most distressing, and no amount of orthoptic training or mental education could remove this annoying condition. Loss in convergence power resulted in the patient's requiring four operations. This loss was due to a bilateral recession of the internal rectus muscles, performed at different operations. The condition was remedied somewhat by a later advancement of one of the internal rectus muscles, but only at a sacrifice of convergence. Various authors have stressed the possibility of this complication. A regrettable loss of convergence often results from (1) too energetic an operative procedure on both internal rectus muscles or (2) too liberal a recession of one internal rectus muscle. Experience has shown me that it is inadvisable either to perform recession of both internal rectus muscles in the same patient or to reinsert a recessed internal rectus muscle posterior to the equator. Thus, a recession of more than 5 mm always entails the possibility of future loss of convergence power. Any remaining deviation is best treated by a future operation on the external rectus muscles.

#### SUMMARY AND CONCLUSIONS

In an analysis of 65 cases of strabismus in adults treated by operative procedures, the following conclusions were drawn:

<sup>18</sup> Linksz, A. The Stereoscope as an Orthoptic Instrument, *Arch Ophth* 26:389-407 (Sept.) 1941.

A proper diagnosis and investigation of the condition of the ocular musculature must be made prior to operation. This can be determined by a routine examination. Included in the study should be measurement of the refractive error, a complete history and determination of the presence or absence of fusion.

Recession of one muscle combined with resection and advancement of the opposing muscle is the surgical procedure which offers the best chance for success.

With proper evaluation of the muscle power and appropriate treatment fusion of some degree will be obtained in 60 per cent of cases.

Amblyopia, suppression, poor fixation and anomalous retinal correspondence constitute definite obstacles in the treatment of strabismus.

Diplopia is a complication resulting from the operative treatment of strabismus.

Joseph Sosnowy, technician fourth class, and Private H. Moskowitz assisted in the examination of the patients in this series.

# BILATERAL TERATOID TUMOR OF THE LIMBUS

CAPTAIN EMANUEL ROSEN

MEDICAL CORPS, ARMY OF THE UNITED STATES

## REPORT OF A CASE

A man aged 25 was first seen at the ophthalmic clinic on Oct 7, 1943, referred because of poor vision in his right eye. Examination was made to determine the patient's physical fitness for full military duty. The patient stated that as long as he could remember vision had been poor in his right eye, that he had never been aware of any acute symptoms involving this eye and that, although its appearance was somewhat disconcerting, it had caused him neither pain nor concern. His left eye had always been normal, never having produced eyestrain and never having required glasses. The family history was insignificant as regards ocular pathologic conditions, no members of the immediate family had had any ocular tumors or other diseases of the eye. His own past history was of no importance ophthalmologically since he had suffered from no unusual diseases of childhood and had never been hospitalized except for a fracture of the wrist.

Examination revealed vision to be 5/200 in the right eye and 20/20 in the left eye. The lids and the lacrimal apparatus were not remarkable, muscle balance was not unusual except for a remote near point of convergence. There was a peculiar dusky red injection of the bulbar conjunctiva, particularly in the right eye. In this eye three fleshy hypervascularized masses were located just on the limbus—two in the upper part of the bulbar conjunctiva and one in the inferior portion of the globe. When the upper lid was everted and the patient looked to the extreme inferior field, these upper fleshy masses seemed to run well up into the cul-de-sac, the temporal lesion joining the region of the lacrimal gland and the nasal mass continuing into the nasal portion of the cul-de-sac. These masses were grayish, slightly elevated and sharply outlined. They extended beyond the corneal limbus for 2 mm. The vascularization increased centripetally. Each mass was approximately 5 mm in diameter. The cornea of this eye was irregularly staphylomatous. With the slit lamp the corneal bulge and the decreased corneal thickness were readily apparent. The anterior chamber consequently was extremely deep at certain sections. There was nothing remarkable about the iris or the lens, the fundus was only indistinctly visualized, for no landmarks could be observed. There was no increase of intraocular tension determinable by means of digital palpation (fig 1).

The left eye showed two smaller masses of similar but less vascular appearance. These masses were located in the upper sector of the globe, with an extension approximately beyond the limbus for 1 mm. There was no scarring of the cornea, no apparent effect on the various radii of curvature and no corneal astigmatism. The remaining ocular structures were all normal.

The general physical examination of the patient revealed nothing of moment. There were no cutaneous tumors and no pigmented nevi or verrucae. The patient had no birthmarks and no congenital anomalies.

There were no aberrations of the skeletal, muscular or nervous system or of other special sense organs which were investigated. The heart, lungs and blood pressure were not remarkable.

Because of the presence of these tumors in the eyes and because of their resemblance to "dermoid tumors" of the conjunctiva, although no cilia were visible anywhere on the tumors, it was decided to perform a biopsy of one of these masses for diagnostic purpose.

The temporal mass in the right eye was dissected free, a local anesthetic being used. The mass was readily removed, with only a moderate amount of

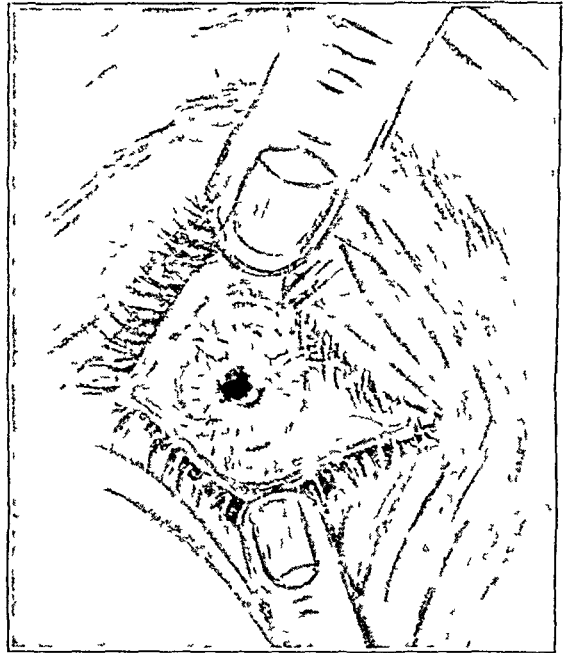


Fig 1—Drawing of right eye, showing three fleshy hypervascularized masses on the limbus.

bleeding. A continuous silk suture, which was removed in five days, was inserted into the conjunctiva for closure of the wound.

The pathologic report was as follows: macroscopically the specimen consisted of a small piece of pale, soft, noncystic tissue measuring 6 by 5 by 5 mm.

Microscopically the section showed a tissue filled with many loose adipose structures, in which there were many islands of lacrimal gland. The adipose tissue took on the form of hexagons, with small, flattened, densely stained, oval nuclei. There were only a few areas of adipose tissue mixed with tissue of the lacrimal gland proper. There were several areas of adipose tissue intermixed with a loose form of connective tissue. The connective tissue in general was loose and laden with many red blood cells and plasma cells, indicative of its extreme vascularity.

There were three large areas of cartilaginous tissue, located at different positions in the section. Each was surrounded by a richly nuclear perichondrium. These cartilaginous islands were located in a zone of loose connective tissue.

There were many islands of glandular tissue. These included alveolar ducts as well as tissue of the gland proper. Most of the cells were vacuolated with the short oval nuclei crowded toward the base of the gland. Most of these glandular masses were embedded in thin adipose and connective tissue (fig 2).

In one small area there was an incomplete section of conjunctiva, which consisted of several rows of epithelial cells located on moderately vascular subconjunctival tissue. An occasional bundle of nerve fibers was seen.

Wilson<sup>1</sup> reported 2 cases of teratoid tumor. The first occurred in a baby boy aged 2 months,

tous capsule was also present. Wilson's second case was reported as a case of dermolipoma or "teratomatous" tumor. This tumor was oval, yellowish and subconjunctival. It had increased slowly in size and had extended just onto the cornea. The excised specimen "consisted of a mass of fatty tissue partially enclosed in a fibrous capsule. There was an elongated narrow strip of normal hyaline cartilage surrounded by perichondrium." The lesion in Wilson's first case represented a form of limbal dermoid frequently associated with coloboma of the upper lid and as such points out the congenital nature of the abnormality, as distinguished from a new growth.

Teratomatous tumors of the lacrimal gland are occasionally misdiagnosed. They have been

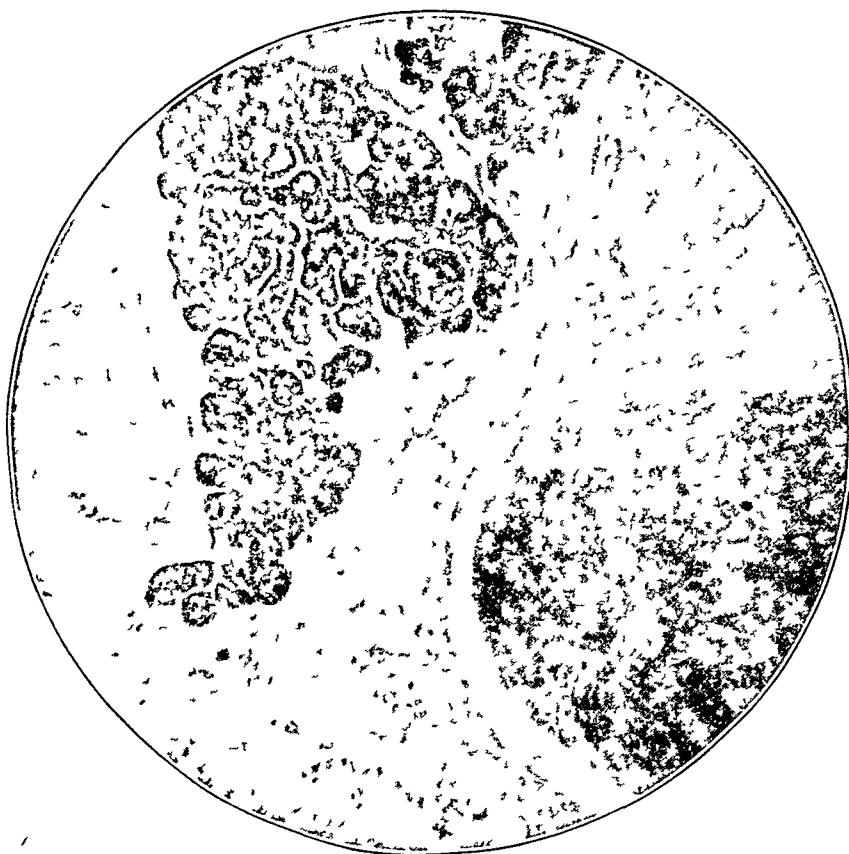


Fig 2—Photomicrograph showing area of glandular tissue with cartilage

who was originally examined because of bilateral congenital notched lids. In the right eye there was a large limbal tumor, which covered the lateral third of the cornea and some of the conjunctiva beyond. A similar but smaller tumor was present in the left eye. These masses were hard and closely adherent to the globe. Microscopically they showed hair follicles and sebaceous glands just beneath the surface epithelium. Cartilaginous tissue surrounded by a fibrolipoma-

called dislocated lacrimal gland, aberrant lacrimal gland with ectopic cartilage, teratoma, mixed lacrimal gland tumor, dermoid, teratoid tumor, and congenital osteoma of the conjunctiva.<sup>2a</sup> A patient with such a tumor may show a defect in the upper lid on the involved side with a peculiar pendulous elongation, which may be pulled down over the eye.<sup>2</sup> In some cases the mass may resemble the not uncommon dermoid of the limbus, but the pathologic section will usually show the true nature of the tumor.

1 Bilateral Dermoid Tumor of Limbus with Bilateral Coloboma of the Lid, in Eighth Annual Report of the Giza Memorial Ophthalmic Laboratory (1933), Cairo, Schindler's Press, 1934, p 54. Dermolipoma of the Conjunctiva Containing Cartilage, in Thirteenth Annual Report of the Giza Memorial Ophthalmic Laboratory (1938), Cairo, Schindler's Press, 1940, p 54.

2 Bon Heeven, J. A. *Nederl tijdschr v geneesk* 72 3566, 1928.

2a Parsons, J. H. *Pathology of the Eye*, New York, G. P. Putnam's Sons, 1908. Snell, S. *Ophth Rev* 1 207, 1881-1882. Coppez, Arch d opht 3 203, 1903. Carter, L. F. *Am J Ophth* 27 67, 1944.

The occurrence of such a tumor at the limbus or nearby has been explained embryologically as a possible remnant of primordial tissue. A dermal inclusion has been suggested as a possible explanation of the site and type of this tumor. Areas of fetal clefts and regions where fetal adhesions might persist and produce pressure have been located. It has been shown<sup>3</sup> that ectodermal inclusion along the lines of the closing facial fissures is not the entire causative factor, although it is usually true that these tumors occur opposite the cranial fetal suture lines.

In 1943 Sherman<sup>4</sup> reported a case of "teratoid tumor of conjunctiva and other developmental anomalies with naevus verrucosus of scalp." The excised tissue showed "serous glands surrounded by loose areolar tissue and dilated endothelial spaces resembling lymphatics with cartilage and

a few nerves cut obliquely and transversely." It was pointed out in the discussion that such growths should be called teratoid tumors. Duke-Elder<sup>5</sup> showed that the usual site is between the external and superior rectus muscles. The presence of a "phacoma" located in the midline in a position occupied by a fetal cleft and associated with a corneal tumor classified as the second type by Ida Mann<sup>3</sup> lends strong support to the theory advanced by Collins and Mayou<sup>6</sup> that these tumors occur opposite the site of bony sutures.

Stargardt<sup>7</sup> suggested that these tumors are congenital anomalies pathologically listed as monophyletic teratoblastomas, since they develop from a single germ layer.

---

3 Mann, I. *Developmental Abnormalities of the Eye*, London, Cambridge University Press, 1937, p. 379.

4 Sherman, A. R. Teratoid Tumor of Conjunctiva and Other Developmental Anomalies with Naevus Verrucosus of Scalp, *Arch Ophth* **29** 441 (March) 1943.

5 Duke-Elder, W. S. *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1937, vol. 2, p. 1411.

6 Collins, E. T., and Mayou, M. S. *Pathology and Bacteriology of the Eye*, ed. 2, Philadelphia, P. Blakiston's Son & Co., 1925.

7 Stargardt, K. *Ztschr f Augenh* **37** 5, 1917.

# INTRINSIC VARIABILITY OF ASTIGMATIC ERRORS

JOSEPH I PASCAL, M D

NEW YORK

The true astigmatic error, as measured in the principal plane of the eye, is not variable in amount, except as all living processes are not absolutely fixed and static. The variability centers on the astigmatic correction which is the astigmatic error in the plane of the lens. Possibly the term "variability of astigmatic correction" would be more appropriate, except that this may be confused with an allied condition.

This variability can best be shown by a few illustrations. Take a patient with 3 D of hypermetropic astigmatism as corrected with a  $+3.00$  D cyl, axis 90. The vertical meridian is emmetropic, the horizontal meridian is 3 D hypermetropic in the plane of the lens. In the principal plane of the eye, say, 17 mm behind the lens, the horizontal meridian is 3.16 D hypermetropic. The true astigmatism, then, which is the difference in refraction between the two principal meridians, is 3.16 D.

When this patient with his correction focuses at a distance of 1 meter from the principal plane of the eye, he is said to accommodate 1 D. As the eye accommodates equally in all meridians, an accommodation of 1.00 D brings the emmetropic vertical meridian in focus for the object. But the same amount of accommodation in the horizontal meridian leaves this meridian underaccommodated by about 0.11 D. To make up this shortage, the eye needs a  $+3.10$  cyl, practically a  $+3.12$  cyl, axis 90.

When this patient focuses at 25 cm and the eye accommodates 4.00 D in all meridians, it is in focus for the emmetropic vertical meridian. But in the horizontal meridian an accommodation of 4.00 D represents an underaccommodation of about 0.42 D, which in the plane of the lens is a deficiency of about 0.44 D. The eye, therefore, needs now a  $+3.44$  D cyl, practically a  $+3.50$  D cyl. The  $+3.00$  cylinder which corrects the astigmatism fully for infinity is about 0.5 D too weak for vision at 25 cm. Thus, a true astigmatism of 3.16 D requires a  $+3.00$  D cyl for vision at 20 feet (6 meters), a  $+3.12$  D cyl for vision at 1 meter, a  $+3.50$  D cyl

for vision at 25 cm and, of course, other powers for other distances.

This variability becomes even more notable if the astigmatism is combined with a spherical error. A patient who has corrected vision with a  $+3.00$  D sph  $\subset +3.00$  D cyl, axis 90, has a true astigmatic error in the principal plane of the eye of 3.51 D, not 3.00 D. When he focuses at 1 meter, he needs a  $+3.00$  D sph  $\subset +3.12$  D cyl, axis 90, and when he focuses at 25 cm, he needs approximately a  $+3.00$  D sph  $\subset +3.50$  D cyl, axis 90. These modified corrections are based on the fact that the over-all accommodation is set by the less hypermetropic meridian. Should the over-all accommodation be set by the more hypermetropic meridian, then the nearest correction for 25 cm is a  $+2.50$  D sph  $\subset +3.50$  D cyl, axis 90. That is, the lens which corrected the eye for infinity is too strong by 0.5 D in the sphere and too weak by 0.5 D in the cylinder when the patient is focusing at 25 cm.

Similar variability, though in a sense in the opposite direction, exists in simple and compound myopic astigmatism. An eye corrected with a  $-3.00$  D cylinder for infinity has a true astigmatism of 2.86 D. When it is focusing on near objects, if the amount of accommodation used is set by the emmetropic meridian, then at 1 meter the eye needs approximately a  $-3.12$  D cylinder, and at 25 cm, approximately a  $-3.50$  D cylinder. Here, again, a true astigmatism of 2.86 D needs a  $-3.00$  D cylinder for infinity, a  $-3.12$  D cylinder for vision at 1 meter and a  $-3.50$  D cylinder for vision at 25 cm. If the amount of accommodation used is set by the myopic meridian, then at 25 cm the needed correction, instead of being  $-3.00$  D cyl, axis 180, is approximately  $+0.50$  D sph  $\subset -3.50$  D cyl, axis 180.

Similarly, in the case of compound myopic astigmatism, an eye with a correction of  $-3.00$  D sph  $\subset -3.00$  D cyl has a true astigmatism of only 2.58 D. When the eye is focusing at 25 cm, the accommodation required in the less myopic meridian is 3.64 D, and that needed in the more myopic meridian is 3.33 D. Whichever meridian determines the over-all accommodation will

cause an excess or a deficiency in the other meridian of about one-third diopter (0.31 D). In the plane of correction this increases to about 0.45 D, or practically 0.5 D.

Other things being equal, the eye will tend to accommodate the minimum amount. Therefore, in cases of simple and compound myopic astigmatism the more myopic meridian is likely to set the pace. This produces a deficiency in the less myopic meridian, equalization of which will need the addition of plus power. The result is a lens which differs both in sphere and in cylinder from the formula for distance.

In cases of mixed astigmatism, the variability of the astigmatism for near vision is still more pronounced. The hypermetropic meridian has to accommodate more than normal, while the myopic meridian has to accommodate less than normal for the same distance. The difference between the two meridians, therefore, becomes more pronounced, so that greater changes in the cylinder are required for near vision. Slight concomitant changes in the sphere may also be required.

How important are these variations? Since it is generally accepted that small astigmatic errors are more apt to cause eyestrain than large errors, it is worth noting that the full correction of an astigmatic error for 20 feet (6 meters) leaves a small variable astigmatic error for every distance within 20 feet.

Another feature of astigmatism which may be considered to be intrinsically variable concerns the axis. The variability is due to any or all of the following factors:

- 1 Cyclophoria. The axis found monocularly, with the eyes dissociated, will be off axis to the extent of the imbalance.

- 2 The compensatory rotation of the eye when the head is tilted to either shoulder.

- 3 The usual binocular extorsion when the eyes change from distant to near vision. This outward rotation of the vertical meridians is so common that it has been termed physiologic, comparable to the so-called physiologic exophoria for near vision. The amount of extorsion varies with the nearness of the object and its position with reference to the horizontal plane. It decreases when the subject is looking below the horizontal plane and increases when he is looking above it. It is therefore of special significance for people who have to use their eyes at close range while looking on a horizontal level or above it. This applies to librarians, tradesmen and others who have to consult items on shelves placed on a level with or above their eyes.

The three aforementioned factors may partly neutralize each other, or they may have a cumulative effect.

#### SUMMARY

An astigmatic eye which is properly corrected for distance develops a variable amount of a new astigmatic error when accommodating for near vision. The amount of this astigmatism, which may be termed induced astigmatism, varies with the amount and kind of the true astigmatism. It also varies with the position of the correcting lens, with the nearness of the object viewed and with whether the amount of accommodation used is determined by the meridian of greatest power or the meridian of least power. The last factor probably depends on the contours of the object looked at. The amount of this induced astigmatism is ordinarily slight but can easily amount to 0.5 D.

A similar variability in the position of the axis is due to the rotation of the eye on an antero-posterior axis, occasioned by three factors: (a) cyclophoria, (b) a compensatory rotation due to tilting the head and, in near fixation, (c) physiologic binocular extorsion. The extent of change in axis is ordinarily low, amounting possibly to 5 or 10 degrees.

There is no way of entirely eliminating the incidence of these intrinsic variabilities. But a few suggestions may be offered:

- (a) When in the usual monocular tests for astigmatism at 20 feet (6 meters) the location of the accepted axis varies within a range of, say, 5 or 10 degrees, it is preferable to choose the axis in line with the physiologic extorsion, that is, the more temporal position.
- (b) Since it is generally more important to have keen, comfortable vision for near than for distant vision, one may obtain a compromise correction by making the astigmatic test at some intermediate near point, e.g., 40 or 50 cm, changing only the spherical element for the 20 foot test, and (c) locating the cylinder axis in each eye during binocular fixation.

Finally, while it is pertinent to know of the existence of induced astigmatism and shifts in axis as occasioned by the factors described, these defects do not in general cause any distress or measurably lessened visual acuity. Possibly the eyes accommodate for the circle of least diffusion, or, more likely, the errors fall within the adaptability of the eye as a living dynamic organ. But for those sensitive patients who are distressed when their correction is off an eighth or a quarter of a diopter, or the cylinder axis is off a fraction of 5 degrees, these considerations should be taken into account.

37 West Ninth-Seventh Street

# FOSTER KENNEDY SYNDROME WITH FUSIFORM ANEURYSM OF INTERNAL CAROTID ARTERIES

I S TASSMAN, MD  
PHILADELPHIA

The location of an aneurysm is the important factor in determining the focal signs. Garvey,<sup>1</sup> in a review of the subject of "Aneurysms of the Circle of Willis," described those aneurysms which arise from the intracranial portion of the carotid artery, from the proximal portions of the middle cerebral artery and from the circle of Willis at the point of bifurcation of these vessels as the anterior group, which presents a remarkably constant clinical picture. Also, because of the higher incidence of aneurysms of the carotid portion of the circle of Willis and the constancy of the clinical picture, the aneurysms in this location are diagnosed more frequently than those elsewhere.

Localized pain in the supraorbital region on the side of the aneurysm may be present for a long time before focal signs appear. Other symptoms resulting from direct pressure on adjacent structures develop, with increase in size of the aneurysm. These may include ptosis, diplopia, intermittent sharp pain over the upper portion of the face and impairment of vision. The oculomotor nerve and less frequently the sensory portion of the trigeminal nerve, the motor division of the trigeminal nerve and the olfactory, optic, trochlear and abducens nerves may be involved by an aneurysm arising from the carotid portion of the circle of Willis. Although compression of the optic nerve on the side of the aneurysm occurs, there may be little evidence of disturbed function.

Many types of defects of the visual field have also been described in cases of such aneurysm. Bitemporal hemianopsia, defects of the nasal field and others have been found.

The case here reported is striking in that it presented a characteristic Foster Kennedy syndrome and, with the exception of pain, almost complete absence of other focal signs and symptoms.

Presented at the meeting of the Section on Ophthalmology, College of Physicians of Philadelphia, Feb 18, 1944.

1 Garvey, P H. Aneurysms of the Circle of Willis, Arch Ophth 11 1032 (June) 1934.

## REPORT OF A CASE

Mrs S F, a white woman aged 32, was first seen by me at Wills Hospital on Nov 17, 1943. She had been referred with a diagnosis of optic neuritis of the right eye and secondary atrophy of the left optic nerve. She was admitted to the hospital on the same day, with the chief complaint of "pain over the right eye and loss of vision in the left eye."

*Past History*—The patient is the mother of two children. She suffered no serious illness until July 1942, when she had a pelvic operation, the exact nature of which is not known.

In April 1943 she suffered with herpes zoster, which affected principally the left side and the back of the neck. There was no history of other illnesses or of injuries.

*Present Illness*—The patient first complained of pain in the left eye in January 1943. She thought she had suffered with a "cold" just prior to this. Shortly afterward, she noticed failure of vision in the left eye. After consulting an ophthalmologist in Reading, Pa., she had some teeth extracted and her sinuses examined. She was hospitalized there and placed under treatment, which included active fever therapy. Vision in the left eye continued to decrease, however, and in October 1943 she began to have pain in the right eye. She then was told that the right eye was also involved. By November 1943 vision in the left eye was almost entirely gone.

*Ocular Examination*—On admission to Wills Hospital, the patient revealed no abnormalities of development or in her general physical makeup. Her head was of normal size and contour. Speech, hearing and smell were not affected.

Vision in the right eye was 6/6 partly, with the left eye she could see hand movements at 12 inches (30 cm). The eyes were in normal position, and the cilia, the lacrimal apparatus and the conjunctiva were all normal.

The action of the lids was good, and no ptosis or nystagmus was noted. The ocular rotations were full in all directions. The pupils, equal in size, measured about 5 mm in diameter. They were round and regular in outline and failed to react to direct light. The anterior chambers were normal in depth, and the tension was normal in both eyes.

Ophthalmoscopic examination revealed the media to be clear in each eye. The right eye showed a definite papilledema measuring about 3 diopters, with marked blurring of the margins of the disk. The retinal veins were enlarged and tortuous, and the arteries were slightly increased in size, but none of the vessels showed any evidence of the presence of an inflammatory process. No hemorrhages, exudates or other pathologic conditions were found in the periphery of the fundus.



In the left eye, the margins of the disk were slightly blurred, the disk was white, with a deep excavation in the center. The retinal vessels showed no evidence of inflammation, and there were no hemorrhages or other pathologic conditions in the periphery. The macula was normal.

The presence of definite papilledema in the right eye with good visual acuity and atrophy of the optic nerve in the left eye with loss of vision suggested a Foster Kennedy syndrome with an intracranial lesion.

**Visual Fields** Examination of the right eye revealed a moderate contraction of the peripheral field and a slight enlargement of the blindspot. There was insufficient vision in the left eye for a test of the visual fields.

**Examination of the Ears, Nose and Throat**—Conditions were normal except for the presence of small and submerged tonsils.

**Röntgenographic Examination of the Skull and Sinuses** (Dr Fetter)—The sella turcica appeared normal and oval, and there was slight calcification in the petrous ligaments.

The bones of the skull were a little thicker than average, but their density was about usual. There was no roentgenographic evidence of increased intracranial pressure, calcification or visible outline of a tumor. The mastoids were moderately developed and had a mixed type of cells, some of which showed considerable thickening of cellular elements.

It was concluded that the skull and the sella turcica showed no evidence of pathologic condition, that mucosal hypertrophy and some exudate could be present in the right ethmoid bones and that slight mucosal hypertrophy existed in the right antrum. The other sinuses were clear.

**Laboratory Studies**—Urinalysis revealed that the urine had an acid reaction, a specific gravity of 1.029. It contained no sugar, but there was sufficient albumin to give it a slightly cloudy appearance. A microscopic examination of the urine showed 25 white blood cells per high power field, many red blood cells, several squamous epithelial cells and amorphous urates.

The blood had a sugar content of 104 mg per hundred cubic centimeters and gave an anticomplementary reaction to the Wassermann test and a negative reaction to the Kahn test.

Examination of the spinal fluid showed a pressure of 110 mm of water, no cells and no globulin and a total protein content of 25 mg per hundred cubic centimeters. The results of a colloidal gold test and Kahn and Wassermann tests were negative.

A Mantoux test gave negative results.

**Neurologic Examination**—The patient was examined by both Dr N. Schlezinger and Dr Bernard Alpers. They suggested the possibility of a suprasellar lesion, either neoplasm or aneurysm, with a Foster Kennedy syndrome. Other localizing neurologic signs were absent.

**Dr Alpers' Report** "I believe this patient has a Foster Kennedy syndrome. The appearance of the right disk seems to me to be that of edema rather than of neuritis. The normal visual acuity in the right eye favors edema rather than neuritis in my estimation. I think the most likely diagnosis is a lesion above the sella turcica, probably compressing the optic nerve and the chiasm. A tumor seems most probable, but multiple sclerosis cannot be excluded. Herpes encephalitis is a possibility, but I am unaware of an encephalitis of herpetic origin secondary to cervical herpes."

In accordance with the recommendation of the neurologist, the patient was transferred to Jefferson Medical College Hospital on Nov 30, 1943, for further studies and neurosurgical treatment.

**Summary of Report of Neurosurgeon, Dr Rudolph Jaeger, Jefferson Hospital** On Dec 2, 1943, encephalography was performed. Routine roentgen study of the skull indicated a normal condition. Roentgen study following encephalography showed no evidence of dilatation of any of the ventricles. The lateral ventricles were symmetric and in the midline. However, there appeared to be a definite lack of sharpness in the extreme anterior portion of the lateral ventricles, which raised the question of possible encroachment on the anterior horn by a suspected suprasellar lesion. In addition, the cisterna chiasmatica, while outlined, was not as large as frequently seen, and this may also have been the result of a mass lesion in this area. The rest of the basal cisterna and the subarachnoid pathways appeared normal.

**Interpretation** In view of the patient's clinical history, the lack of good filling of the extreme anterior horn and the small size of the cisterna chiasmatica raised the question of a large suprasellar lesion (Teplick).

**Reports on Visual Fields** (Dec 2, 1943)—No field was obtained with the left eye. In the right eye there were slight concentric constriction and slight enlargement of the blindspot, with visual acuity of 20/30.

**Report of Operative Procedures**—Craniotomy (Dec 14, 1943). A flap of bone was turned down over the left frontal lobe. There were no adhesions about the optic nerve or strictures around the chiasm. The left nerve was of normal size and appearance. It was entirely free and not compressed by any visible lesion. Just beneath it was a fusiform aneurysm of the internal carotid artery, which after emerging from the base of the skull formed a complete loop into the region of the sella turcica and then passed backward to its normal location to progress laterally to the middle cerebral artery. It appeared as though the artery was bound to the base of the skull by the ophthalmic artery. On the right side there was a similar fusiform aneurysm, with a mass of tiny veins on it, just beneath the optic nerve. This pressed the optic nerve backward tightly against the posterior edge of the optic foramen. It was impossible to do anything surgically with the lesion. It is believed that ocular difficulty on the left side was caused by sclerosis of the ophthalmic artery, because obviously there was not enough pressure against the optic nerve to cause atrophy and blindness. The pressure against the optic nerve on the right side was definite enough to cause progressive blindness, although one would think there would be atrophy rather than edema of the disk on that side. The pressure, however, may have been just sufficient to cause congestion of the venous blood returning from the orbit. The roof of the orbit over the top of the optic nerve should have been removed to relieve the pressure against it, but it was impossible to do this through the left frontal lobe. This should be kept in mind so that the procedure may be carried out by an operation through the right frontal lobe, should blindness set in and become progressive. The whole chiasm and both optic nerves were completely exposed without difficulty. The bone flap was wired in place after the dura was tightly closed. The skin was sutured with silk, with a Penrose drain beneath the flap.

**Postoperative Diagnosis** The diagnosis was bilateral fusiform aneurysm of the internal carotid artery

**Report on Visual Fields (Jan 6, 1944)** No field was obtained with the left eye. There was marked concentric constriction in the right eye. Visual acuity was 20/70. **Arteriography (Jan 14, 1944)** The right carotid arteries were exposed. The external carotid artery was temporarily occluded. Fifteen cubic centimeters of 35 per cent diodrast solution was injected rapidly into the internal carotid artery. Roentgenograms taken after this showed a tortuous internal carotid artery just beneath the right optic nerve, as observed at a previous operation. An aluminum clip was loosely placed around the internal carotid artery, in order to occlude this vessel later, if it seemed to be advisable.

**Postoperative Diagnosis** The diagnosis was fusiform intracranial aneurysm of the internal carotid artery on the right side.

**Craniotomy (Jan 19, 1944)** A flap of bone was turned down over the right frontal lobe. The right optic nerve was exposed without difficulty. The internal carotid artery fitted snugly beneath it and pressed it rather tightly against the upper edge of the optic foramen. A part of the vessel could be seen to the left of the optic nerve. The roof of the optic canal was removed for a distance of about  $\frac{1}{2}$  inch (1.27 cm) from the foramen. The left optic nerve was visualized and appeared to be more snugly pressed against the edge of the foramen than was obvious at the first operation. The right optic nerve appeared to be of good bulk and was not as tightly constricted as it should be to produce the loss of vision which occurred. Apparently the visual loss had to do at least partly with the papilledema caused by venous congestion. The dura was sutured tightly. The bone flap was wired in place and the muscles and skin closed with silk.

**Postoperative Diagnosis** The diagnosis was fusiform aneurysm of the carotid artery.

**Further Course (Jan 24, 1944)** The aluminum clip which had been placed about the right internal carotid artery was removed. It appeared to have completely occluded the internal carotid artery, owing to adhesions, although the clip was by no means tightly closed. The wound was sutured with silk.

**Report of Visual Fields (Jan 29, 1944)** No field was obtained with the left eye. In the right eye there was further constriction of the visual field. Visual acuity was 5/200.

#### SUMMARY

A married woman aged 32 suffered with pain over the eyes and loss of vision in the left eye over about eight months. Other subjective signs and complaints were practically absent. Ocular examination revealed the presence of a Foster Kennedy syndrome (papilledema with good

vision in the right eye and atrophy of the optic nerve and almost total loss of vision in the left eye). The presence of a suprasellar lesion was suspected. Definite diagnosis was made at the time of operation, which revealed bilateral fusiform aneurysms of the internal carotid arteries, with formation of anomalous loops in the course of the arteries and compression of the optic nerves.

#### CONCLUSION

This case was considered to be of especial interest to the ophthalmologist from the standpoint of the ocular involvement that was revealed and the lack of other major signs and symptoms.

Since it was first described by Foster Kennedy,<sup>2</sup> or perhaps even earlier by Paton,<sup>3</sup> the syndrome has been considered to indicate the presence of a basofrontal tumor. However, a number of cases have been reported since that time in which it was present with non-neoplastic conditions. One of these was a case of aneurysm of the right internal carotid artery later reported by Kennedy himself. Most of the others were cases of arteriosclerosis or atherosclerosis of the vessels with compression of the optic nerves. H. E. Yaskin and N. S. Schlezinger<sup>4</sup> described 2 such cases and referred to about 11 others which they found in the literature associated with various other conditions. Among these was 1 (Cusick) which was reported in association with a tumor of the cerebellum. The ocular changes in this case were said to be caused by extreme dilatation and forward displacement of the third ventricle.

Because of the anomalous vascular condition found at the time of operation, it is felt that the case here reported is one of congenital origin.

2 Kennedy, F. Retrobulbar Neuritis as an Exact Diagnostic Sign of Certain Tumors and Abscesses in the Frontal Lobes, *Am J M Sc* **141** 355, 1911.

3 Paton, L. A Clinical Study of Optic Neuritis in Its Relationship to Intracranial Tumors, *Brain* **32** 68, 1909.

4 Yaskin, H. E., and Schlezinger, N. S. Foster Kennedy Syndrome Associated with Non-Neoplastic Intracranial Conditions, *Arch Ophth* **28** 704 (Oct) 1942.

# PATHOGENESIS OF ACUTE GLAUCOMA

LEO HESS, M D

BOSTON

"Like the eyes are not to be treated without the skull and the skull is not to be treated without the entire body, the body is not to be treated without the soul. The Greek physicians fail to cure many diseases because they ignore the entire entity of man. If the entire body does not feel good, a part of it cannot be improved."

—Plato, Charmides 156 E

It is generally agreed that the clinical signs of acute "inflammatory" glaucoma are caused by increased intraocular pressure (Fuchs<sup>1</sup>). Treatment is directed, in accordance with this classic teaching, toward lowering the tension, in order to avoid damage to the tissues of the eyeball, particularly to the optic nerve. The cause and the mechanism of the increased tension are still unexplained. In an earlier paper<sup>2</sup> I expressed the view that the pathologic hardening of the eyeball with glaucoma is analogous to the physiologic orgasm, both events being dependent on reactions within the vegetative nervous system. The integrated clinical picture, with its numerous signs, viewed broadly may be regarded as a vegetative neurovascular crisis, other examples of which are epileptic seizures (particularly the type occurring during digestion, which can be described as a 'sympathetic crisis') and attacks of cardiac asthma associated with acute edema of the lungs (Hess<sup>3</sup>).

An outstanding clinical sign of acute glaucoma is venous congestion of most of the tissues of the eye. Dilated venous loops in the center of the optic disk are not uncommon. A "head of Medusa" may occasionally be observed in the bulbar conjunctiva. The veins of the orbit communicate with many venous sinuses and plexuses nearby, all richly endowed with nervous plexuses and ganglion cells. These elements are presumably important for the regulation of the venous blood stream within the bulbus. The arterial branches of the eyeground are frequently

narrowed and the delicate temporal rami may altogether disappear. This narrowing of the arterioles cannot be adequately accounted for by increased intraocular pressure. It is more likely that it is caused by increased activity of certain vasomotor nerves. The immediate effect of arteriolar constriction and partial ischemia is dilatation of the capillaries and later of the smallest veins (Krogh<sup>4</sup>). The rise in intra-capillary pressure and the dilatation of the capillaries and of the nearby venules is necessarily associated with the escape of plasma by filtration, with increase of the fluid content of the bulbus. It appears that the relationship between the increased intraocular pressure, on the one hand, and the vascular changes, the increased transudation of fluid and finally the so-called glaucomatous atrophy of the optic nerve, on the other hand, is not as simple as some investigators are inclined to suppose.

## SIGNS OF ACUTE GLAUCOMA

It is necessary to analyze the main signs and symptoms of acute glaucoma briefly in order to establish a theory of pathogenesis which can account for the entire clinical picture on a rational basis.

*Hardening of the Eyeball*—Hardening of the eyeball in glaucoma is caused by an increase in the content of fluid with resulting occlusion of the angles of the chamber and congestion of the choroid, sclera and conjunctiva. The increase in the content of fluid may be the result of increase in the arterial blood supply, of impairment of the venous return or of both. In addition to these factors, the increase in capillary transudation is to be borne in mind. In physiologic hardening, as exemplified by the orgasm, both factors operate without resulting transudation. Since there is no evidence of arterial hyperemia in glaucoma, venous congestion remains for consideration. The occurrence of the prodromes and of the attacks after hearty meals, after emotion and in association with objective signs of heart failure suggests that venous congestion plays a precipitating role.

4 Krogh, A. *The Anatomy and Physiology of Capillaries*, ed 2, New Haven, Conn, Yale University Press, 1929

Dr Hess was formerly Professor of Medicine and Neurology at the University of Vienna.

Dr Boruchoff and Dr Elsberg, of the Eye Clinic of Beth Israel Hospital, gave assistance in this study.

1 Fuchs, E. *Lehrbuch der Augenheilkunde*, Leipzig, Franz Deuticke, 1939, p 426.

2 Hess, L. *Pathology of Acute Glaucoma*, Arch Ophth 26 250 (Aug) 1941.

3 Hess, L. *Deutsches Arch f klin Med* 173 283, 1932.

However, it cannot be denied that a primary, transient rise in the blood pressure, for example, after nervous strain, may antedate the venous congestion

The bearing of venous congestion on the causation of glaucoma is illustrated by the following report on a case

H A, a 41 year old housewife, had nosebleed for a week. The bleeding was stopped by cauterization. Some years previously she had had hematometra as a result of constriction of the cervix of the uterus. Menstrual bleeding was irregular and occasionally prolonged. She had pains in the right flank and hematuria. Compensated heart disease was present. The patient was adipose, with a flushed "full moon" face, and the veins on both sides of the neck were slightly distended.<sup>5</sup> The veins of the conjunctiva were tortuous and congested, especially in the left eye, and the retinal veins were lightly tortuous. Small points and streaks appeared in the lens. There was no cupping of the optic disk, and the peripheral fields were normal. The intraocular pressure was 56 mm (Schiotz) in the right eye and 75 mm in the left.

Consistent with the hypothesis of venous congestion as a cause of glaucoma are the well known conditions observed in ophthalmoscopic examination after an attack. Simultaneous arterial narrowing and venous distention can be explained satisfactorily as a neurovascular phenomenon.<sup>6</sup> Primary constriction of the arterioles may give rise to reflex dilatation of capillaries and veins (Krogh<sup>4</sup>), along with increased transudation of fluid. Glaucoma due to thrombosis of small branches of the ophthalmic vein, with secondary collateral dilatation of other veins and increased intraocular pressure was described by Magitot and Bailliart.<sup>7</sup>

*Mydriasis*—Dilatation of the pupil is a common and impressive sign before and during attacks of glaucoma. At first it is transitory, but it may last for several days and in the advanced stages of the disease may become permanent. Similar persistent mydriasis may be elicited by instillation of atropine in the eyes of patients with sympathicotonia.<sup>8</sup> Not only is the pupil of the involved eye much larger than the other pupil, but it is sometimes oval rather than round, and it may be eccentric. The dilated, oval pupil does not react to light or accommodate for distance. These findings suggest a hyperactive or spastic condition of the

dilator muscle of the iris, which is innervated by sympathetic fibers. In the early stages this hyperactivity must be functional, because it is transitory, later it is persistent and must be caused by an organic lesion.

Sympathetic stimulation of the dilator muscle of the iris may arise in the diencephalon, in spinal centers or in peripheral sympathetic fibers or ganglions. Karplus and Kreidl<sup>9</sup> described a vegetative center in the diencephalon not far behind the optic tracts and lateral to the infundibulum. Stimulation of this area in animals results in maximum dilatation of the pupils, widening of the eye slits, retraction of the so-called inner lid, lacrimation and vasomotor reactions. Budge<sup>10</sup> described the ciliospinal sympathetic center, at the level of the eighth cervical and first and second thoracic segments of the spinal cord. From the ciliospinal center arise certain fibers which reach the superior cervical ganglion and pass by way of the carotid plexus to the gasserian ganglion. From there they course via the ophthalmic branch of the trigeminal nerve and the long ciliary nerves to the vessels of the eyeball, the dilator muscle of the iris and the mullerian muscle. These are the so-called peripheral sympathetic fibers of the eye.

In which part of the sympathetic system may the stimulus producing glaucoma arise?

There is no reason to suppose a mechanical irritation of the peripheral sympathetic fibers or ganglions such as may be produced by enlargement of the cervical or mediastinal lymph nodes or of the thyroid gland. Nor is there evidence of chemical stimulation, such as is produced by excessive secretion of epinephrine, as occurs with sympathoblastoma. Functional hyperactivity of the peripheral portion of the sympathetic nervous system would involve, according to the concept of Eppinger and Hess,<sup>8</sup> the entire system. But in glaucoma the nervous disturbance is limited to the eyeball and the surrounding structures (conjunctiva and lids), the inner organs apparently being exempt.

A central origin, either within the spinal cord or within the brain, must be considered. Mydriasis due to irritation of the ciliospinal center is rare except as a result of injury at birth, and it is associated with involvement of the cervical or the thoracic portion of the spinal cord, which is absent in glaucoma. Accordingly, a cerebral factor must be considered, perhaps

5 The venous congestion reminds one of the "plethoric" facies seen in patients with Cushing's syndrome (adrenal cortical hyperfunction).

6 As early as 1846 Taignot suggested a nervous disorder of the ciliary body as a cause of glaucoma.

7 Magitot, A, and Bailliart, P. *Ann d'ocul* **162** 729, 1925, *Am J Ophth* **8** 761, 1925.

8 Eppinger, H, and Hess, L. *Ztschr f klin Med* **68** 205 and 230, 1909.

9 Karplus, I P, and Kreidl, A. *Arch f d ges Physiol* **129** 138, 1909, **135** 401, 1910, **143** 109, 1911, **171** 192, 1918, **215** 667, 1927.

10 Budge, J. *Ueber die Bewegungen der Iris*, Braunschweig, Fr Vieweg u Sohn, 1855, chap 4.

involvement of the center described by Karplus and Kreidl. The clinical findings are consistent with the effects of stimulation of this center.

In addition to mydriasis, which is absent only rarely, a slight bulging of the bulbus may sometimes be noticed in patients with glaucoma. The widening of the interpalpebral fissure is probably masked by the acute swelling of the lids and the conjunctivas.

The sympathetic nervous system produces "crises" analogous to that of glaucoma, as has already been suggested.

In this relation I should like to cite a case reported by Wallenberg<sup>11</sup>. The patient had hypotonia, atrophy and chorea of the muscles of the right arm and leg, anhidrosis of the right half of the body and mydriasis and enlargement of the eye slit of the right eye. The organic lesion was in the right side of the base of the brain close to the right corpus subthalamicum, that is, in the vicinity of the Karplus-Kreidl center. The oculopupillary syndrome resulting from the diencephalic lesion is remarkable evidence in support of the assumption that mydriasis associated with glaucoma is of cerebral origin.

The condition known as "hemicrania sympathica" is a phenomenon related to glaucoma, characterized by pallor of one half of the face, cordlike contraction of the temporal artery (it is "like pieces of wire" according to Lauder Brunton), dilatation and fixity of the homolateral pupil, production of a small amount of tenacious saliva ("sympathetic saliva") according to Ludwig), high pulse rate, one-sided headache and vomiting. The veins of the retina may be engorged and its small arteries constricted. The similarity of this condition, which is generally agreed to be dependent on increased sympathetic influences, to acute glaucoma, except for the changes within the eye, is obvious.

Epileptic seizures likewise bear numerous signs of sympathetic crises (fixed, large pupils, general pallor, sometimes failure of the peripheral pulse at the beginning of the attack and constriction of the retinal arteries). The origin of the sympathetic hyperactivity in migraine and in epilepsy needs further investigation. Suffice it to say that all of these conditions are the result of sympathetic stimulation. If it is assumed that the primary site of the lesion in acute glaucoma is within the diencephalon, all the main signs must be logically accounted for on this basis. In addition to the diencephalon,

the ciliary ganglion, as an important reflex center of the eyeball, deserves full attention.<sup>2</sup>

**Headache**—Patients with glaucoma complain of frontal headache or of pain in one temple, radiating to the upper jaw or to one ear. The type of headache is that of intracranial neuralgia of the trigeminal nerve, simulating the pain of migraine. Central stimulation of the Karplus-Kreidl center could easily result in referred pain in this region. The stimulus may spread from there through the peduncles to the cervical portion of the spinal cord, to the ciliospinal center (Budge<sup>10</sup>) and finally, through the rami communicantes, to the sympathetic trunk. It may be conveyed by sympathetic fibers, arising from the first cervical ganglion of the sympathetic trunk, to the gasserian ganglion. The unilateral headache with nausea and vomiting remind one of migraine, especially as many patients with glaucoma, like those with migraine, keep their eyes closed and prefer a dark room. Headache, nausea and vomiting may persist for one or two weeks after the attack, and the clinical picture reminds one of gastric crisis due to tabes dorsalis, the nervous origin of which is not doubtful. Nausea may be the premonitory sign of a new attack of glaucoma.

**Hyperthermia**—Since there is no infection or demonstrable toxic agent, it may be inferred that the hyperthermia that occasionally accompanies acute glaucoma is of central origin. An important heat-regulating center is located in the area of the tuber cinereum, which is close to the Karplus-Kreidl center. This heat-regulating center is made up of a sympathetic and a parasympathetic portion. Sympathomimetic drugs (tetrahydronaphthylamine, epinephrine, ephedrine, caffeine and cocaine) cause a rise of temperature by specific stimulation of certain cells within the heat center, and the parasympathomimetic drugs (pilocarpine, picrotoxin, veratrine and santonin) are able to reduce the temperature of the body through their specific action on other cells in the same center. High temperature may be encountered without any infection as a result of central stimulation in heat prostration, cerebral hemorrhage close to the third ventricle, exerting mechanical pressure on the tissue below the third ventricle, including the tuber cinereum, hydrocephalus, injury to the brain, and epilepsy. The Karplus-Kreidl center is likewise believed to be built up of two antagonistic portions. High temperature with glaucoma could therefore result from the same mechanism that operates in the production of fever with injury of the brain, cerebral hemorrhage, hydrocephalus and epilepsy.

<sup>11</sup> Wallenberg, H, cited by Muller, L. R. *Lebensnerven und Lebenstrieb*, Berlin, Julius Springer, 1931, p. 181.

*Photophobia*—Photophobia is a reflex phenomenon arising from irritation of the cornea, conjunctiva or iris, mediated by the trigeminal nerve. It represents hypersensitivity of the retina, which Claude Bernard<sup>12</sup> demonstrated even in blind men and in animals in which the optic nerve was severed. The sensitivity of the retina is decreased by instillation of parasympathomimetic drugs. The sedative action of cocaine is dependent on its action on the terminations of the trigeminal nerve, abolishing the sensory part of the reflex arc.

*Chemosis*—Chemosis and swelling of the eyelids might be signs of inflammation, but their similarity to angioneurotic edema and to acute pulmonary edema accompanying organic lesions of the brain (Hess)<sup>13</sup> leads us to suggest a neural origin. With inflammatory conditions of the eye, for example, iritis, the intraocular pressure is lowered.

*Lacrimation*—Lacrimation during and sometimes following acute glaucoma is analogous to the profuse lacrimation noticed by Kaapalus and Kieidl on stimulation of the diencephalic center.

#### INDIRECT EVIDENCE OF THE INTERVENTION OF A NERVOUS FACTOR IN THE PATHOGENESIS OF ACUTE GLAUCOMA

*Periodicity*—Glaucoma exhibits a periodicity resembling that seen in attacks of migraine, cardiac asthma, epilepsy and the attacks of pain and vomiting of gastric crises due to tabes dorsalis.

*Bilateral Involvement*—Bilateral involvement, even though the intervening interval may be long, indicates not a local, but a central, nervous disturbance.

*Association with Emotional Disturbances*—Undoubtedly there is a relationship between glaucomatous attacks and emotional disturbances (anxiety, fear or worry). Sometimes glaucoma develops in one eye after an operation on the other. Indeed, under conditions of anxiety, increase in the size of the pupils, enlargement of the interpalpebral fissure, slight bulging of the eyes and spasm of the retinal arteries, signs similar to those of acute glaucoma, may be observed.

*Relation to Sleep*—According to some investigators the influence of the parasympathetic nerves prevails during sleep. Sleep would therefore represent a natural balance against the hyperactivity of the antagonistic sympathetic

nerves. With glaucoma sleep is often disturbed, but the relief of pain, chiefly of the glaucomatous headache, that occurs rarely during sleep reminds one of the similar relief of migraine. It is not without significance to recall the deep sleep that follows the sympathetic crisis of an epileptic seizure.

*Trophic Changes*—The neural origin of the so-called "trophic" changes is beyond any doubt, although the mechanism is still obscure, despite the important work by Parker<sup>14</sup>.

*Spontaneous Recovery*—Spontaneous recovery, particularly from the prodromal symptoms, is not unusual. Oddly, it is accompanied with a drop in the intraocular pressure to a point below the normal level (to about 15 Schiøtz units). The rise and fall of the tension cannot be accounted for except by a nervous mechanism.

*Association with Ophthalmic Herpes Zoster*—Herpes zoster ophthalmicus may antedate an attack of acute glaucoma. This condition is accompanied with unilateral neuralgia referred to the eye, eyebrow and forehead, edema around the eye and sometimes with mydriasis. The neuralgia is apparently intracranial, its primary site is believed to be in the gasserian ganglion.

In one of my patients an inflammatory condition of the cornea was followed by glaucoma.

*Bilateral Extension of Symptoms*—The intraocular pressure of the normal eye may rise to some degree during an attack of glaucoma.

*Relation to Fever*—Febrile disease of various sorts may precipitate attacks of glaucoma. The relationship is hard to explain satisfactorily, but frequently during febrile episodes the equilibrium of the vegetative nerves is disturbed, with the sympathetic influence prevailing.

#### PHARMACOLOGIC ASPECT

It is hardly necessary to note that if atropine sulfate is instilled into the fornix of a glaucomatous eye an acute attack may ensue, presumably the atropine inhibits the action of acetylcholine and permits sympathetic dominance. The action of atropine lasts much longer in a glaucomatous than in a normal eye, owing to the fact that the hypoactivity of the parasympathetic nervous system can more easily be overcome. For contraction of the pupil of an untreated glaucomatous eye or after the use of atropine much stronger solutions of pilocarpine, physostigmine and mechoyl are required, which demonstrates that the parasympathetic tone is low as compared with the normal and that stronger stimulation is needed.

<sup>12</sup> Bernard, C. Leçons sur la physiologie et la pathologie du système nerveux, Paris, J-B Baillière, 1858, vol 2, p 90

<sup>13</sup> Hess, L. Wien med Wchnschr 84 285, 1934

<sup>14</sup> Parker, G. H. Humoral Agents in Nervous Activity, New York, The Macmillan Company, 1932

In one of my patients the pupil, contracted by pilocarpine, expanded suddenly during the night and no longer responded to pilocarpine. The change occurred during the first day of profuse metrorrhagia. Instillation of procaine hydrochloride may produce dilatation of the pupil and increase in intraocular pressure. In some cases hypersensitivity to procaine is striking. In some instances of acute glaucoma, after instillation of epinephrine hydrochloride (1:1000 solution) the pupil becomes dilated. This reaction—the so-called Lowy phenomenon—is evidence of unblocked sympathetic hyperactivity (Hess<sup>15</sup>).

After administration of caffeine by mouth (a cup of black coffee), the pressure in a glaucomatous eye may rise above the normal level, this facilitates early diagnosis, since a normal eye would not show any change. The rise in pressure is evidence of increased irritability of the nerves. The action of caffeine is complicated. It acts on the heat center at the base of the brain (Barbour and Wing<sup>16</sup>), on the vasomotor center and on the muscular walls of the arteries of the brain (Roy and Sherrington<sup>17</sup>).

A histamine-like substance was found by Friedenwald<sup>18</sup> and by Raycroft<sup>19</sup> in the aqueous humor of glaucomatous patients. The same finding has been recorded by Kirwan<sup>20</sup> for patients with epidemic dropsy, characterized by high temperature, diarrhea, anemia, edema of the legs and acute glaucoma.

15 Hess, L. Epinephrine Mydriasis, *Arch Ophth* **30** 194 (Aug) 1943

16 Barbour, H. G., and Wing, E. S. *J Pharmacol & Exper Therap* **5** 105, 1913

17 Roy, C. S., and Sherrington, C. S. *J Physiol* **11** 85, 1890

18, Friedenwald, J. S. Pathogenesis of Acute Glaucoma, *Arch Ophth* **3** 560 (May) 1930

19 Raycroft, B. W. *Brit J Ophth* **18** 149, 1934

20 Kirwan, cited by Magitot and Baillart<sup>7</sup>

At first glance it is surprising that in some patients with glaucoma the tension is greatly reduced after instillation of pilocarpine or physostigmine, whereas in normal eyes the tension remains unaltered (Traquair<sup>21</sup>). In these patients apparently the primary sympathicotonic condition produced, by means of a reflex, secondary hypertonia of the antagonist. These signs of counterbalance are not too rare and are confusing to the inexperienced. A similarly "paradoxical" reaction is the absence of mydriasis in late cases of glaucoma.

Miosis of the pupils, seen with syphilitic conditions of the spinal cord, is, according to my observations, not seldom associated with extreme slowness of response to atropine, probably as a result of hyperactivity of the parasympathetic fibers. This phenomenon is the reverse of the long-lasting response to atropine in glaucomatous eyes.

It is noteworthy that after an attack of glaucoma the response to miotic drugs is more pronounced than during the attack.

#### CONCLUSIONS

- 1 Acute glaucoma is a neurovascular crisis.
- 2 The vegetative diencephalic center at the base of the brain (the Karplus-Kreidl center) and the ciliary ganglion play predominant roles in the nervous mechanism of glaucoma.
- 3 Increased intraocular pressure and many signs of acute glaucoma are secondary to the central irritation.
- 4 The so-called inflammatory signs of the attack (dusky redness of the conjunctiva, chemosis, edema of the lids and changes in the cornea) are of angioneurotic origin.

15 Kenwood Street, Brookline, Mass

21 Traquair, H. M. *Brit M J* **2** 933, 1935



# Clinical Notes

## EFFECT OF DIETHYLSTILBESTROL ON ACCOMMODATION

LEO L. MAYER, M.D., ST. LOUIS

Clinical research and practical observation at times may call the attention of members of the medical profession to deviations from the normal without providing an insight into the basic physiologic and pathologic changes. This report serves such a function. It lacks a bibliography, a history of the use of diethylstilbestrol or a discussion of the phenomenon of accommodation. Since I have seen accommodative changes in cases in which diethylstilbestrol has been used for several years and have found no previous report of such a case in the literature, it seemed wise to record representative cases for the enlightenment of ophthalmologists and endocrinologists.

Since the advent of the use of diethylstilbestrol or similar androgens for the relief of symptoms of sexual dysfunction in females, or more usually of disturbances of the menopause, I have examined about 40 women with complaints which, when analyzed, were found to be due to difficulties in accommodation. Of this number, I report here the cases of 5, which are representative with respect to symptoms and treatment of five types under which the majority of such cases would fall.

It is well known that presbyopia and the menopause occur in the same or in the preceding or the succeeding decade. My impression when I first began to see patients with difficulties in accommodation was that of precocious presbyopia or premature menopause or both. Gradually, I realized that most women with menopausal symptoms were "taking shots" or were receiving glandular preparations by mouth, and finally I took persistent steps to assure myself, in spite of the patient's answer to the contrary, that she was receiving endocrine therapy, "which could have little to do with the eyes." Such an attitude is characteristic of most patients, as well as of some physicians, who feel that the eyes constitute a separate and distinct portion of the body, unrelated to any other bodily mechanism. It soon became apparent that such reactions were found not only in women with beginning presbyopia but in those who had worn reading glasses or bifocal lenses for several years. Of course the outstanding complaint of the majority of patients was difficulty of near vision. Ordinarily, the answer to this is the prescription of reading glasses, or a

change in the strength of the glasses the patient is already wearing. However, when I, or some other ophthalmologist, had changed the lenses three or six months before, further investigation was indicated.

During the past four or five years I have inquired of many ophthalmologists whether they had encountered such cases in their experience and have never had a positive answer. However, during the past year I have had letters and personal communications from physicians who have kept my question in mind and wished to tell me of their experience.

### REPORT OF CASES

CASE 1—Mrs. L. F., aged 38, was emmetropic on examination six years before. Recently she had had difficulty in reading telephone numbers. The past and present histories were without significance except for painful menstruation, for which she had been "taking shots" during the previous month. Examination showed that vision for distance was normal in each eye. Ophthalmologic examination revealed nothing abnormal except that the near point for accommodation was 10 inches (25 cm). As she appeared too young for presbyopia, I consulted her gynecologist, who agreed to discontinue the injections of diethylstilbestrol. In one week her accommodation returned to normal, the near point being 6 inches (15.2 cm). Examination six months later showed no change. The painful menstruation was being treated with antispasmodics.

CASE 2—Miss G. Y., aged 43, had never worn glasses. During the week prior to examination she had noticed a blur before the right eye. Visual acuity was 20/20 in the right eye and 20/30 in the left eye. There was no central scotoma. The visual fields were normal. The fundi were normal. Refraction gave a correction of +0.5 D sph for the right eye and of +0.75 D sph  $\ominus$  0.50 D cyl, axis 90 for the left eye. The near point of accommodation for the right eye was 9 inches (22.9 cm), and that for the left eye, 7 inches (17.7 cm). The patient was given daily doses of 1½ grains (0.097 Gm) of diethylstilbestrol, and 1 grain (0.065 Gm) of thyroid, the latter for mild "flashes." The administration of diethylstilbestrol was discontinued, and in two weeks the near point of accommodation for either eye, and for the two together, was 7 inches (17.7 cm).

CASE 3—Mrs. G. H., aged 53, had had difficulty with near vision for two weeks. I had her glasses changed four months before and had changed the prescription two years prior to that correction. She had received injections of diethylstilbestrol biweekly during the past year. The additional correction for accommodation two years ago was a +2.75 D sphere. At the last refraction she accepted a +3.75 D sphere to bring the near point to 7 inches (20.4 cm). Injections were reduced to one a month. The patient had a blood pres-



sure of 220 systolic and 140 diastolic. She did not feel as well after the injections were reduced and wanted them increased. After two months' trial the new reading correction, which was rechecked, was accepted.

CASE 4—Miss P. P., aged 16, had difficulty in focusing her eyes while reading. She had severe dysmenorrhea. She had received increasing doses of diethylstilbestrol by injection during the preceding six months, with some relief of the menstrual condition. Visual acuity for distance was normal in each eye. There was bilateral weakness of accommodation. The near point of accommodation was 15 inches (38 cm) for each eye. With a correction for reading of a +3 D sphere for each eye, the near point of accommodation was 8 inches (20.4 cm). Injections of diethylstilbestrol were stopped. Accommodation returned to normal in three months.

CASE 5—Mrs. K. T., aged 57, had had her glasses changed four times by four ophthalmologists during the previous year. She was unable to see fine print at normal reading distance with her present glasses. No change in the lens or in the vitreous could be detected. There was no history or clinical indication of diabetes.

She had been taking diethylstilbestrol hypodermically and by mouth for the past four years, for relief of "hot flashes." An increased correction of 1 D was required in her reading glasses. Medication was discontinued for two weeks, with complete recovery of normal accommodation for a person of her age.

In June 1942 the Council on Pharmacy and Chemistry of the American Medical Association<sup>1</sup>

<sup>1</sup> Diethylstilbestrol, report of the Council on Pharmacy and Chemistry, *J. A. M. A.* **119** 632 (June 20) 1942.

reported on diethylstilbestrol, citing several articles which noted undesirable reactions of the drug. The following symptoms, listed in the order of frequency of their occurrence, were stated to accompany the use of diethylstilbestrol: nausea, vomiting, headache, vertigo, abdominal distress, diarrhea and dermatoses. No mention was made of any ocular reactions.

Whether similar changes in the accommodation apparatus have occurred with the newer synthetic estrogens, such as triphenylethylene,<sup>2</sup>  $\alpha\alpha$ -di(par-aethoxyphenyl)- $\beta$ -phenylbromoethylene<sup>3</sup> and octofollin (2,4-di[parahydroxyphenyl]-3-ethylhexane),<sup>4</sup> I have been unable to determine. Just what physiologic changes occur in the accommodation apparatus with the use of diethylstilbestrol has not been worked out. It is felt that the report of these cases may induce others to study this phenomenon.

634 North Grand Avenue

<sup>2</sup> Robson, J. M., and Schonberg, A. Estrous Reactions, Including Mating, Produced by Triphenyl Ethylene, *Nature*, London **140** 196 (July 31) 1937.

<sup>3</sup> Robson, J. M., and Schonberg, A. A new Synthetic Estrogen with Prolonged Action When Given Orally, *Nature*, London **150** 22 (July 4) 1942.

<sup>4</sup> Blanchard, E. W. Responses of Laboratory Animals to a New Synthetic Estrogen, *Endocrinology* **30** 1026 (June) 1942.

## Obituaries

CARL FISHER, M D  
1879-1944

Dr Carl Fisher, one of the outstanding ophthalmologists of the West, died in Los Angeles on June 7, 1944, after a prolonged chronic illness

I first met Carl Fisher when he came to practice his specialty in Los Angeles, in 1921. I well remember the great sense of pride we of the

Carlton College, Northfield, Minn., and received his degree of Doctor of Medicine from Harvard Medical School in 1905. His internships were at the Carney, the Massachusetts General and the Infants' Hospital, Boston, and his basic ophthalmologic training was at the Massachusetts Eye and Ear Infirmary. He left Boston in 1909



CARL FISHER, M D  
1879-1944

medical profession felt in welcoming to Southern California such a nationally known ophthalmologist, former chief of the eye, ear, nose and throat section of the Mayo Clinic (1909 to 1917). He brought to our community the best in ophthalmologic experience and professional tradition. He had recently returned from study in Europe, subsequent to active overseas duty in the Army in World War I.

Carl Fisher was born July 16, 1879, in Breckenridge, Minn. He graduated in 1901 from

to accept the position at the Mayo Clinic, in which he became nationally known.

The medical societies of which he was a member included the American Board of Ophthalmology, the American Ophthalmological Society, the American College of Surgeons and the American Academy of Ophthalmology and Otolaryngology.

When he came to Los Angeles, these accomplishments led to his becoming an influential member of the local societies. He became clinical

professor of ophthalmology at the University of Southern California School of Medicine, a position he filled with active interest up to the time of his death

Although not a prolific writer, his mental endeavors in the form of lectures, letters, discussions and clinical appraisals were gems of clear thinking, concise and pointed. Carl Fisher was blessed with one of the keenest intellects in the profession.

This attribute, plus his personal qualities, made him the ideal consultant, always contributing something of value to a solution of the problem and having that unusual knack of self effacement which allowed him to help the physician more than to impress the patient.

Because of his wisdom, common sense and unprejudiced desire to understand conflicting points of view, he was the final arbitrator in disputes and dissension arising within the local societies. He had a mild manner, inconsistent with that of an ardent crusader, preferring to exert his influence through subtle suggestion and exemplary professional conduct. It was characteristic of him to be tolerant of points of view relative to practice which, as judged by his own conduct, were distasteful to him.

He was thoroughly human, enjoying life fully and possessing a delightful sense of humor. This made him the preferred toastmaster and impromptu speaker. His repertory seemed inexhaustible and invariably reflected his sensitive and cultured tastes. He was a devotee of activities in art and music in the community.

One of his chief local interests was the Research Study Club of Los Angeles, of which he was one of the founders. He always attended the formal meetings and took an active part in the

informal gatherings that followed. At these there was much jocular repartee, in which he had no peer. It was on such occasions that his culture, high ideals and way of enjoying life were manifested to his colleagues and made their mark on the younger men of the organization.

Carl Fisher's philosophy of life can best be portrayed through a chance remark made to me while visiting him at the hospital the day before his death. We were talking about the war, the coming invasion and places in France he knew so well, when he said something to this effect: "You know, it is strange that I, who am about to become an estate so soon, should be so interested in all the trivialities that occur about me. I really can't help being as curious and as interested as I ever was."

To those of us who knew him he will never be "just an estate," but one whose friendship enriched our lives by teaching us how to live. Perhaps the fact that he never married enabled him to give more freely of his friendship and time to the welfare of his colleagues than would otherwise have been possible.

A RAY IRVINE

---

## News and Notes

---

### PERSONAL NEWS

**Appointment to University of Oregon Medical School**—Dr. Kenneth L. Swan, who for the past five years has been connected with the medical department of the State University of Iowa College of Medicine, has been made associate professor of ophthalmology at the University of Oregon Medical School, and assumed his new duties on July 10.

# Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

---

## Congenital Anomalies

A CASE SHOWING PARTIAL DEFICIENT FUSION OF A MAXILLARY PROCESS WITH LATERAL NASAL PROCESS ON ONE SIDE G E DODDS, Brit J Ophth 27:414 (Sept) 1943

A Negro girl aged 3 months presented the congenital abnormalities to be described. The outstanding defect was distortion of the right nostril with a hiatus showing the interior of the nose, the cleft extending upward to within 1 cm of the inner canthus, which had a wide, obtuse angle. There were small notches, or colobomas, in both upper lids and a notch in the right lower lid. There was no caruncle, and the presence of a plica semilunaris was doubtful. On the inner side of the medial canthus of the left eye there was a vertical hole, in appearance like the opening of a sinus. The cleft, or fissure, extended from the lower and lateral margin of the right nasal bone to a point where normally the nostril joins the lip. This was merely a cleft in the cartilaginous part of the nose. The eyes were normal in every respect.

A sketch accompanies the article

W ZENTMAYER

## Cornea and Sclera

HEREDITARY CORNEAL DYSTROPHY J R MUTCH, Brit J Ophth 28:49 (Feb) 1944

The subject of hereditary corneal dystrophy is considered fairly exhaustively. It is pointed out that Groenouw first described the disease in 1890 under the term "nodular corneae." That the disease is familial was first noted by Fuchs, in 1901. Mutch advocates the use of the descriptive term "granular" dystrophy and suggests that the term "nodular" be abandoned because it has caused so much confusion. He gives a pedigree in which 24 members were affected, of the affected, 14 were males and 10 females, the youngest was a boy aged 12 and the oldest 90 at the time of examination. Eight of the affected members were over 60 when examined. Fourteen of the patients were myopes. Mutch is inclined to think that the low myopia or myopic astigmatism was due in some cases to the corneal lesions but that in others the myopia was due also to heredity and was connected with the corneal disease. Up to the age of 50 corrected vision was in no instance less than 6/12. The visual acuity, however, does not suffer an irresistible diminution with the advance of age, as 4 affected patients, well over 60, still have

vision of 6/12 or better. Only 1 patient, a man over 90, could have been certified as blind. In an old granite polisher the corneas had the appearance of hereditary dystrophy. The lesions, however, were all on the surface, but appearance of the eye and the distribution of the opacities were exceedingly similar. The lesion is not granular corneal dystrophy if it is unilateral, shows signs of vascularity, opacities are visible on examination with the naked eye in a patient under 30 and there is absence of a similar condition in both parents. The author considers the condition as probably a nutritional disturbance. The cornea receives its nutrition from the vascular loops at the limbus, lymph permeating centrally between the layers of the corneal lamellae. Any error in this circulation of lymph would affect the area farthest from the supply, namely, the central region of the cornea. Weight is given to this argument by the observation of several investigators (Bucklers), who stated that considerable improvement followed an intercurrent inflammation with vascularization of the cornea.

The progress of the disease was not brought to a standstill with certainty with any form of treatment used, far less was the disease made to retrogress. In certain cases the attempted cure was more harmful than the disease.

The refractive error should be corrected with glasses and the refraction periodically checked. The general health should be kept at as high a level as possible, with careful attention to diet, supplemented by the periodic addition of vitamins A and B.

The article is illustrated, and an excellent bibliography is appended. W ZENTMAYER

## General

AN OPHTHALMOLOGIC REVIEW OF MORE THAN TWENTY THOUSAND MEN AT THE ALTOONA INDUCTION CENTER L P GLOVER and W R BREWER, Am J Ophth 27:346 (April) 1944

Glover and Brewer present a table of refractive and congenital defects, traumatic injuries and ocular diseases. They give the following summary:

"Of 21,446 men going through the Altoona Induction Station, a total of 21.36 per cent had eye defects that lowered vision to 20/40 or less. This, excepting hyperopia, represents a fair cross section of eye defects in central Pennsylvania."

W S REESE

## General Diseases

OCULAR ROSACEA AND ARIBOFLAVINOSIS W  
M FISH, *Am J Ophth* 27. 354 (April)  
1944

Fish reviews and compares his work with that of Wise and of Johnson and Eckardt, in general agreeing with Wise that rosacea is not a manifestation of riboflavin deficiency

W S REESE

## Injuries

WAR INJURIES OF THE EYE TRAUMATIC PROLIFERATIVE CHOROIDITIS DUE TO DOUBLE PENETRATING FOREIGN BODY I C  
MICHAELSON and J KRAUS, *Brit J Ophth* 27 449 (Oct) 1943

In 6 of 7 cases of injury to the eye by a foreign body with an exit wound in the posterior part of the globe, the fundus had the following appearance after the vitreous had cleared sufficiently to permit detailed ophthalmoscopic study. A white mass of varying size could be seen in the area of choroidoretinal atrophic change. The whiteness was often milky and was sometimes glistening, with a few dots of crystalline brightness on the surface. The mass looked solid and in some cases projected far into the vitreous. It was not usually crossed by retinal arterioles or venules. Dark pigment might cover a part of its surface.

In the seventh case the fundus could not be seen on ophthalmoscopic inspection. In 2 cases in which pathologic studies were made the clinical appearance at the posterior wound appeared to be based on a massive proliferation.

The article is illustrated

W ZENTMAYER

FIRST AID TREATMENT OF INDUSTRIAL EYE INJURIES R M DICKSON, *Brit J Ophth* 27: 544 (Dec) 1943

The great majority of the injuries were caused by a fragment of steel or iron in the cornea, but brass, copper, aluminum and gun metal also played their part. Next in importance were foreign bodies from abrasive wheels. Burns from acids and sodium hydroxide were common in chemical factories, and there were a few cases of conjunctivitis from mercury fulminate. The author gives the following summary:

"This report deals with 2,478 eye injuries in 30 collieries in Scotland extending over a period of eighteen months, and 11,953 eye injuries in 30 factories in Scotland in six months.

"First aid treatment was essentially the use of 10 per cent albucid soluble (sodium sulphacetamide) as eye drops.

"Of the total injuries in collieries, 96 per cent returned to work with no loss of working time.

"In factories and shipyards, there was no loss of working time in 98.87 per cent of the cases.

"These eye drops have already been recom-

mended by the Ministry of Fuel and Power for use as first aid treatment in collieries throughout the country.

"The excellent results after six months' trial in factories fully justify the recommendation that the new eye drops be adopted in all forms of industry where there is any danger of injury to the eyes."

W ZENTMAYER

## Neurology

THE OCULAR MANIFESTATIONS OF SPONTANEOUS SUBARACHNOID HEMORRHAGE A J  
BALLANTYNE, *Brit J Ophth* 27 383  
(Sept) 1943

Since in the majority of cases of subarachnoid hemorrhage the hemorrhage comes from the vessels of the circle of Willis, being due to the rupture either of an aneurysm or of a weakened portion of the vessel wall, the effusion of blood may be relatively slight but is likely to recur. The chief symptom in such cases is severe, deep-seated pain, often accompanied by paresis of one or another of the ocular muscles. Arteriographic studies of the brain may reveal the presence of an aneurysm, and lumbar puncture may disclose blood in the cerebrospinal fluid.

In the cases of severe hemorrhage, such as those reported in this paper, the clinical picture is entirely different. The patient is seen in a more or less comatose state, with a history of sudden onset and with signs suggestive of cerebral compression and meningeal irritation, pupillary anomalies, nystagmus, conjugate deviation of the eyes and paralysis of cranial nerves, including those supplying the extraocular muscles are often observed. These signs are not in themselves sufficient to justify a diagnosis of subarachnoid hemorrhage. The presence of retinal hemorrhages and papilledema, if observed on ophthalmoscopic examination, strongly supports such a diagnosis and a history of minor attacks adds to its probability, but the matter is settled by the discovery of blood in the cerebrospinal fluid.

Five fatal cases of spontaneous subarachnoid hemorrhage are described with special reference to the pathologic condition of the eye and its related structures.

The discovery of hemorrhage in the subarachnoid space at the base of the brain, within the sheaths of the optic nerve, and in many cases in the retina and even in the vitreous, originally led to the belief that the blood passed in a continuous manner in the subarachnoid space through the optic canal into the orbit and thence either along the course of the central retinal vessels or by lymph channels accompanying the optic nerve at the periphery of the lamina cribrosa into the retina.

It is not generally agreed that the blood in the cerebral subarachnoid space does not, as a rule, travel through the optic foramen into the subarachnoid space of the optic nerve. It is

more generally assumed that hemorrhage occurs in the dural sheath at the apex of the orbit and tracks forward into the subdural and the subarachnoid space, and that blood in the subarachnoid space, by exerting pressure and tension on the central retinal vein where it crosses the space, causes stasis in that vein and thus accounts for the hemorrhages in the retina and vitreous

On the basis of the 5 cases described here, it is shown that hemorrhages occur over a much wider field than the optic nerve sheaths, the retina and the vitreous and that these hemorrhages cannot be accounted for by the assumed pressure on the central retinal vein

The hemorrhages varied in distribution from case to case but were noted in and between the sheaths of the optic nerve, in the orbital fat and among the orbital muscles and around the posterior ciliary nerves, the ciliary ganglion, the ophthalmic and posterior ciliary arteries and the vessels of the chiasm and optic tracts, as well as beneath the retina, in all its layers, in front of the retina and in the vitreous. Serial sections showed that these hemorrhages were not continuous one with another but were discrete and independent, of simultaneous occurrence. It is submitted that the occurrence of such multiple hemorrhages can only be explained by a sudden rise of intracranial pressure, causing stasis in all the venous channels which drain the tissues of the eye and the contents of the orbit

It is suggested that some of the clinical signs of subarachnoid hemorrhage, such as oculomotor pareses and disturbances of the conjugate movements of the eyes, may be explained by the occurrence in the midbrain of hemorrhages similar to those observed in the chiasm and the optic tracts in 1 of the cases

W ZENTMAYER

ATAXIC NYSTAGMUS A PATHOGNOMONIC SIGN IN DISSEMINATED SCLEROSIS W HARRIS, Brit J Ophth 28:40 (Jan) 1944

Harris gives the following description of the sign "When the eyes are turned laterally, the conjugate action appears weak, so that the inner eye, e g, the right eye when looking towards the left, does not reach the inner canthus, but the outer eye shows coarse nystagmus, the eye reaching the outer canthus with a quick movement, and a slower return, as though the outward movement could not be maintained, owing to weakness. Usually the nystagmus of the outer eye continues as long as the patient looks in that direction, the inner eye meanwhile remaining stationery, not having quite reached the inner canthus. It is this discrepancy between the movements of the two eyes which suggests to the author the term 'ataxic nystagmus'.

"Usually this peculiar nystagmus will be present when looking either to the right or left, though it may be more marked in one lateral

movement than in the other, or it may be seen only in one lateral direction"

W ZENTMAYER

## Orbit, Eyeball and Accessory Sinuses

A CASE OF MONOCULAR HYDROPHTHALMIA, WITH SPECIAL REFERENCE TO ITS POSSIBLE RELATION TO THE STURGE-WEBER SYNDROME A GARROW and A LOEWENSTEIN, Brit J Ophth 27:335 (Aug) 1943

A case of monocular hydrophthalmia in a girl aged 11 years is described. She was first seen at the age of 5½ years, when the condition was typical hydrophthalmia, involving the right eye. Cyclodialysis and two trephinations were done at various times, with resulting hypotonus, but later the eye was removed because it began to shrink. Besides the many changes due to the hydrophthalmia, three angiomas were noted—the first in the choroid at the posterior pole surrounding the optic nerve, the second in the retina near the optic nerve and the third in the anterior part of the eye in connection with the choroid.

The authors discuss the relation of such a condition to the Sturge-Weber syndrome and suggest that angioma of the choroid may be the connecting link between the two diseases.

Calcification of the ocular tissue (capillaries, angiomas, internal limiting membrane and ganglion cells) was a feature of the case.

Reference is made to the allied anomalies—von Recklinghausen disease, Treacher Collins—von Hippel-Lindau disease and Bourneville's disease.

An angioma of the retina recently observed in a case of Bourneville's disease is briefly described.

The article is illustrated with photomicrographs of the pathologic features.

W ZENTMAYER

## Physiology

THE SIGNIFICANCE OF THE DISTRIBUTION RATIOS OF NON-ELECTROLYTES BETWEEN PLASMA AND THE INTRA-OCULAR FLUID STEWART DUKE-ELDER and H DAVSON, Brit J Ophth 27:431 (Oct) 1943

The authors state that for readers to whom a mathematical argument has no appeal the general problem with which this article deals may be stated thus. If the concentration of a given substance, urea for instance, is higher in the blood than in the aqueous humor, the system, plasma-aqueous humor, is not in equilibrium, and hence diffusion of urea should take place into the aqueous humor until the condition of equilibrium of equal concentrations in the two fluids is achieved. Kinsey and Grant admitted that this would happen in the absence of drainage and secretory activity. However, they

claimed that as soon as drainage occurs the concentrations become different, i. e., the system is no longer in equilibrium so far as urea is concerned, as defined thermodynamically

The second law of thermodynamics states that a system of this kind can be maintained at a position of nonequilibrium only by the continued performance of work on it. Drainage of fluid away from the anterior chamber is not capable of performing the necessary work on the system, so that in the absence of secretory activity the differences in concentration claimed by Kinsey and Grant are excluded. W ZENTMAYER

### Retina and Optic Nerve

THE HEREDITARY MACULAR DEGENERATION  
R I LLOYD, *Am J Ophth* 26: 499 (May) 1943

Lloyd describes four types of hereditary macular degeneration. In the first, and most common, form large white spots are scattered about the macula, and the condition is described in the literature as honeycomb, or guttate, choroiditis. The second type, in which many small white dots are scattered about the fundus, most numerous in or limited to the periphery, is usually described as retinitis punctata albescent. The third type appears under the term juvenile maculocerebral degeneration. A fine pigment is seen in the macular area, with thinning of the choroid. In the fourth type the appearance is that of disappearance of some of the layers of the choroid. The edges of the defect are sharp, the sclera is not bared, but long, straight choroidal vessels are uncovered. In some cases there is little pigment, and in others clumps of heavy pigment are present. The peripheral part of the choroid may resemble gyrate atrophy of the choroid and retina, or a type of choroideremia.

The article is illustrated. W ZENTMAYER

TWO CASES OF VISIBLE EMBOLI IN RETINAL ARTERIES, WITH A HISTOLOGICAL STUDY IN ONE CASE. W E C DICKSON, G C PRITCHARD, L H SAVIN and A SORSBY, *Brit J Ophth* 28: 1 (Jan) 1944

After a review of the clinical histories of the 2 cases in which actual emboli could be seen in the retinal arteries, the authors discuss several points in the cases. They believe that the white background was due to ischemic necrosis of the ganglion cell and nerve fiber layers rather than to mere edema and that massage shifted the embolus in the first case. In the second case the patient claimed subjective improvement in vision, but no accurate estimate was possible. Histologic examination of the eye of the second patient showed round cell infiltration of the optic nerve, choroid and retina, of the subacute or chronic variety, the block in the artery was an embolus, of some duration, lodged in a vessel

with a slight or moderate degree of previous thickening of its tunica media and adventitia, but not of its intimal coat. There were localized proliferative thickenings of the intima in the immediate neighborhood of the embolus, which was just beginning to be canalized by the invasion of endothelial buds in its periphery. The changes in the retina, both proliferative and irritative, were not extensive and were most evident in the inner layers. These changes probably dated from the time of impaction of the embolus. There were recent acute changes in the choroid. The histologic evidence by itself was conclusive enough, but taken together with the clinical and pathologic evidence as a whole—the cardiac lesion with vegetations, the multiple embolic processes and the absence of arteriosclerotic changes and thrombus formation—leaves no valid doubt as to the nature of the block.

The article is illustrated. W ZENTMAYER

### Tumors

CANCER OF THE EYELID. L HOLLANDER and F J KRUGH, *Am J Ophth* 27: 244 (March) 1944

This article represents a study of 125 cases of cancer of the lid. The impression was gained that most satisfactory results were obtained from scalpel excisions or contact roentgen irradiation, with use of a special shield.

W S REESE

TUMOR OF THE LACRIMAL GLAND. J J FLICK, *Am J Ophth* 27: 362 (April) 1944

Flick reports a case of tumor of the lacrimal gland which was incompletely removed by means of an osteoplastic flap over the left frontal lobe. The pathologist reported that the neoplasm showed features of adenocarcinoma.

W S REESE

OPTIC-NERVE ATROPHY IN MALIGNANT NASOPHARYNGEAL TUMORS. M R FOLK, *Am J Ophth* 27: 373 (April) 1944

Folk reaches the following conclusions:

"Involvement of the optic nerve in malignant tumors of the epipharynx is not frequent."

"The optic atrophy in the cases herein described is preceded by invasion of the epipharyngeal tumor into the sphenoid sinus. This fact explains why the appearance of the optic atrophy is late."

"From the sphenoid sinus the malignant tumor may invade the optic nerve after perforating the lateral wall of the sphenoid sinus."

"The dural sheath of the optic nerve as well as the periosteum of the orbit and the dura is more resistant to aggression by the tumor than is bone tissue. This holds true for sarcoma."

W S REESE

### Visual Tracts and Fields

THE FORM AND CHARACTER OF ROD SCOTOMETRY P C LIVINGSTON, *Am J Ophth* 27: 349 (April) 1944

Livingston gives the following summary

"Scotometry, employing self-luminous test objects and a red fixation light, appears to reveal defects in the central field of vision which cannot readily be found by customary procedures. It is well to confine this method to the 30-degree screen. Up to this point, it is possible to work with very low luminosities, such as  $4 \times 10^{-9}$  or  $6 \times 10^{-9}$  candle power, without introducing physiologic effects likely to be confused with early pathologic conditions. Further work is being undertaken to improve equipment and technique, so as to establish normal field characteristics."

W S REESE

### Vitreous

DISCUSSION OF TRAUMATIC HYALOID DIAPHRAGM J FOSTER, *Brit J Ophth* 27: 462 (Oct) 1943

A bomb explosion caused multiple perforating injuries to both eyes due to fragments of glass, resulting in loss of the left eyeball and reduction of vision in the right eye to good light projection. In the right eye the lens was clear. Examination of the fundus showed a large hemorrhage and detachment of the retina in the nasal area. Later a gray haze behind the lens prevented a further view of the fundus. A membranous diaphragm being suspected, several months later the membrane was divided from in front with a Ziegler knife. Cataract subsequently

developed. Two discussions were made, and ultimately vision with correction was 6/5. Almost two years later the condition of the eye was unaltered.

W ZENTMAYER

### Therapeutics

THE SULPHONAMIDES IN EXPERIMENTAL OCULAR INFECTIONS M KLEIN and A SORSBY, *Brit J Ophth* 27: 241 (June) 1943

Klein and Sorsby give the following summary

"The problems involved in the experimental study of ocular chemotherapy are indicated, stress being laid on the absence of a satisfactory technique for the organisms commonly met with in ocular infections and on the levels of concentration that different sulphonamides reach and maintain in ocular tissues by the general and local administration of these drugs.

"A review of the literature on experimental chemotherapy by general and local administration of the sulphonamides is given.

"Work is recorded which substantiates the claims for sulphanilamide in controlling experimental intra-ocular infection with *Streptococcus haemolyticus* and possibly also *pneumococcus B*. *pyocyaneus* infections of the cornea were not controlled either by the general administration of sodium sulphacetamide or by the use of this drug in a variety of ways as a local application.

"In the absence of a more standard technique of inducing experimental infection of the cornea, the problem of the relative value of general and local use of the sulphonamides remains unsolved. The value of local therapy is still an open question."

W ZENTMAYER



# Society Transactions

EDITED BY DR W L BENEDICT

## AMERICAN OPHTHALMOLOGICAL SOCIETY

JOHN GREEN, M D, *President*

WALTER S ATKINSON, M D, *Secretary*

*Seventy-Ninth Annual Meeting, Hot Springs, Va, June 10-12, 1943*

**Further Experiences with a System of Intracapsular Extraction of Cataract** DR DANIEL B KIRBY, New York

This article was published in full, with discussion, in the April 1944 issue of the ARCHIVES, page 302

**Keratoconjunctivitis Sicca** DR SANFORD R GIFFORD †, DR IRVING PUNTENNEY (by invitation) and DR JOHN BELLOW (by invitation), Chicago

This paper was published in full in the August 1943 issue of the ARCHIVES, page 207

### DISCUSSION

DR WILLIAM P BEETHAM, Boston Up to 1934 only 40 cases of filamentary keratitis had been reported This paper shows how easy it is to see something when one begins to look for it In my opinion filamentary keratitis is just another form of keratoconjunctivitis sicca In 1934 I described a method of destroying the lacrimal puncta in an attempt to make better use of what tears are available I found it difficult to keep the canaliculi closed I used the actual cautery and the diathermy current, and I found that after weeks or months the canaliculi became recanalized, so during the past few years I have resorted to Dr Verhoeff's suggestion of excising the lateral half of each canaliculus

In applying the Schirmer test for tearing, I have always inserted the filter paper over the lacrimal puncta, and I have set as a standard 15 mm of moistening in five minutes I always measure the 5 mm which I tuck into the conjunctival sac

Dr Gifford did not mention his criteria for destruction of the canaliculi It has been my impression that if there is moistening of 10 mm or more in five minutes the patient will be comfortable without resort to surgical treatment, but if the moistening is less than 10 mm, I suggest destruction of the canaliculi by excision of the external half of each

† Dr Gifford died February 25

It is interesting to me that this condition is seen chiefly in females In all of the 40 cases I found reported in the literature up to 1934 the patient was a female In the papers by Sjogren and Bruce and in Dr Gifford's paper, there have been a few cases of males In all the cases I originally reported the patients were females, and I know of no case of the disease in a male, but I think I have been missing some cases of the mild form which Dr Gifford has described

DR RALPH I LLOYD, Brooklyn I wish to speak of 2 cases of this condition Case 1 was that of a young girl on whom Dr Charles Rosenthal operated for dermoid just beyond the lateral rectus muscle The mass extended well down into the orbit, and healing was uneventful A month later the characteristic symptoms of filamentary keratitis appeared These were promptly relieved by use of the moist chamber spectacle, which she lays aside now and then, only to have prompt return of all the annoying symptoms This case suggests that damage to the ciliary ganglion caused the disease

The moist chamber spectacle will do all that surgical closure of the canaliculi will do, and I expected that Dr Beetham would mention the device, as it seems to have originated in Boston Locke's solution, buffer solutions and castor oil have all failed to help the few patients I have treated

Case 2 was that of a single woman aged 45 who had been troubled for about a year with what was diagnosed as keratitis sicca The Schirmer test showed the same rate of secretion (7 mm) in the apparently normal eye as in the offending eye The moist chamber spectacle is of great comfort to her, but every now and then a relapse occurs, at which time fine filaments are seen on the cornea The only associated conditions are the menopause and a cutaneous condition, which has not yet been diagnosed

DR ARNOLD KNAPP, New York It was formerly taught that removal of the lacrimal gland was feasible and that the action of the mucous cells in the conjunctiva was sufficient to preserve the integrity of the cornea, in fact,

at one time the operation of removal of the accessory lacrimal gland was a popular one for relief of tearing after extirpation of the lacrimal sac

Did Dr Gifford observe a definite lesion of the conjunctival epithelium in his cases?

DR ALBERT L. BROWN, Cincinnati I should like to cite several cases of this interesting condition, on the basis of a possible etiologic factor. In 1 case the condition developed after an operation on the gasserian ganglion, the entire cornea becoming involved about five weeks later. In another case it followed direct trauma to the cornea from a scratch by a dog's nail. This accident caused a minor abrasion, apparently rather superficial, which cleared in a reasonable time, from ten days to two weeks, in about three weeks the cornea began to break down and presented a typical picture of dry cornea, with diminished lacrimal secretion. In 3 cases of mixed tumor of the lacrimal gland no sign of corneal involvement appeared after operation, in 1 case, in particular, I removed a great proportion of the gland five years ago, but the cornea has remained clear.

DR LAWRENCE T. POST, St. Louis I wish to speak of those cases in which there are corneal changes and the Schirmer test shows not more than 1 mm of dampness on the exposed filter paper. I have been so much impressed by the presence of a glandular deficiency in most of these cases that I have made it a routine to prescribe a glandular preparation, theelin for the women and testosterone for the men, in the relatively small group of patients I have treated. In addition, I have given vitamin A routinely, 50,000 units a day, and have instilled haliver oil in the eye three times a day. A woman with a particularly severe form of the disease, who had had to stay in a dark room for three years and had not been able to carry on any work because of her eyes, was much relieved by the intravenous injection of antimony and potassium tartrate. She was given injections of this substance because of its known beneficial effect on epithelium. I have had her under observation since, for four or five years, during which time she has been able to work and has been relatively free from discomfort.

DR FRANCIS H. ADLER, Philadelphia Tears are equivalent to about a 1.4 per cent solution of sodium chloride. My associates and I have not had enough cases of this condition to try hypertonic solutions. In the cases we have had we have used an artificial solution of tears comparable in tonicity to blood, in view of Cogan's work, however, I suggest the use of a hypertonic solution, which is equivalent to a 1.4 or 1.5 per cent solution of sodium chloride.

DR NELSON M. BLACK, Miami, Fla. In the investigation of these cases, did Dr Gifford make any attempt to determine the blood picture and the basal metabolic rate?

DR SANFORD B. GIFFORD, Chicago I am glad that Dr Beetham was able to discuss the paper, for, as every one knows, he was the first to close the canaliculi in order to relieve keratitis sicca. I agree with him in almost everything he said except with respect to the method of making the Schirmer test. When I looked up Schirmer's description of the test, I found that he did it as I have indicated. Dr Beetham records the 5 mm of the paper that is turned over. That portion is almost always wet. I measure from the border of the lid down, if he were to set 10 mm of wetting as his criterion for destruction of the canaliculi, it would correspond to the 5 mm as I measure it, this is the criterion I use, except that I also take into consideration the clinical picture of my patient. The patients of group I showed a slight lacrimal deficiency, with no corneal changes, and those of group II, slight corneal changes, so treatment depends chiefly on the severity of the corneal lesions associated with a lacrimal deficiency of 5 mm on repeated tests. As a therapeutic test the puncta may be closed temporarily with trichloroacetic acid. There is no increase in lacrimal secretion after destruction of the puncta, but retention of the tears in the sac gives the patient great relief.

A moist chamber spectacle may be of value in cases of extreme deficiency of tears. Our patients never get complete relief, but it is remarkable how much relief they do obtain. They are always a little sensitive to light. I have a patient now—who is getting only moderate relief. Her vision is reduced to 20/100 as a result of the repeated occurrence of small corneal lesions, these have not healed after closing of the puncta. Some patients have permanent scarring. While the lesions are epithelial, they seem to produce notable reduction in vision.

Dr Knapp asks about the epithelium. I have not made any sections but can see the thickening. It resembles that in trachoma. The epithelium must show a pathologic change.

Dr Post mentioned glandular therapy. In my paper I described the use of theelin and thyroid for a few patients who showed a low metabolic rate, and Dr Puntenney made a complete chemical analysis of the blood in a few cases. He did not find anything of significance except an increased sedimentation rate, with moderate anemia in some cases. He also made examinations for the vitamin A content of the blood and found no deficiency. However, we give vitamin A by mouth, as Dr Post does. We do not think it has any value in local treatment.

I am surprised that in Dr Brown's cases of tumor of the lacrimal gland keratoconjunctivitis sicca did not follow operation, that can be explained only on the ground that some of the gland, either the accessory or the main gland, or at least some of the ducts, must have been left. One usually has complete keratitis sicca, as I did in a case of lymphosarcoma, in which it was necessary to remove some of the conjunctiva in that region.

Dr Adler's suggestion is a good one, and I shall try it.

#### Subjective Experience with Epidemic Keratoconjunctivitis DR THOMAS D ALLEN, Chicago

I infected my own eyes in a moment of pre-occupation. Vision deteriorated during a period of three weeks until it was 20/200 or less in each eye. The physical signs were classic and were confirmed by a number of the members of this society. Treatment was of no avail until a preparation of vitamin C was given intravenously. Vision was slowly restored to normal. The psychologic reaction was at first disturbing.

#### DISCUSSION

DR F C CORDES, San Francisco. Epidemic keratoconjunctivitis appeared for the first time in San Francisco in August 1941. There is no question that the disease is contagious. In California it is known as "shipyard conjunctivitis" and is considered an industrial disease. In my opinion, it is so called because it occurred in persons working in close quarters in the shipyards, where one shift went off as the next came on and the men handled equipment which had previously been contaminated. The severity of the keratitis varies tremendously. In some patients it lasts a relatively short time and clears up without difficulty. With others it has taken a year and a half for the opacities to clear sufficiently for vision of 20/20. Of the patients I have seen, there is 1 whose vision has not improved beyond a questionable 20/40. I tried all types of therapy, without any apparent benefit. Dr J W Crawford, who has seen the largest number of patients in San Francisco, had a similar experience and stated that the use of cold compresses gave the greatest relief. Patients with the more severe type of keratitis seem to retain changes visible with the slit lamp, even though vision has returned to normal. These changes consist of fine annular scars, similar to those described in cases of keratitis nummularis.

DR JOHN N EVANS, Brooklyn. For two years I have been using a preparation of 1 per cent paredrine hydrobromide with 2 per cent boric acid for a variety of pathologic disturbances

of the epithelium, such as bullous keratitis, superficial punctate keratitis and keratoconjunctivitis. It seems to me that I have gained a therapeutic advantage by so doing. I have not observed any opacities in a small number of cases of "shipyard conjunctivitis." This may be a coincidence. I am not making a positive statement as to the value of this treatment, but I suggest its trial. I have had 3 cases of so-called virus pneumonia in the immediate families of patients with epidemic conjunctivitis.

DR PETER C KRONFELD, Chicago. Except that a colleague and friend was concerned, Dr Allen's case was not unusual. It emphasizes the important fact that the onset of epidemic keratoconjunctivitis may be gradual and non-characteristic. During the first two days of Dr Allen's stay at the hospital my associates and I were not at all sure of the diagnosis. On the third day the situation had become obvious.

In this connection, it may be of interest to cite the histologic report by Gunther (*Klin Monatsbl f Augenh* 103:309, 1939). A patient one of whose eyes had been blind for a number of years as the result of a retinal detachment presented himself at an ophthalmic clinic in Berlin with bilateral epidemic keratoconjunctivitis, with the request that the blind, painful eye be enucleated. Histologically, subepithelial infiltrations and areas of degeneration of Bowman's membrane were noted. Gunther stated that the latter lesion was primary.

DR HAROLD HENRY JOY, Syracuse, N Y. A rather mild epidemic occurred in Syracuse. I saw about 25 cases. What impressed me in my series was the scattered distribution of the cases. Few were associated with any particular industry, and in only 1 instance did I know of direct infection from one patient to another.

In 5 cases the condition was unilateral, and in at least 3 of these the patient was not one who would be careful about protecting the uninvolved eye.

DR JOHN H DUNNINGTON, New York. I have a patient with this disease who has been under my care for the past six months, and his vision is still 20/200. There have been several others whose corneal lesions have been present for as long as a year. I am convinced that some of the therapeutic measures employed in Dr Allen's case must have had a beneficial effect.

DR C A CLAPP, Baltimore. I raise the question of the possibility that the virulence of this infection subsided as it swept over the country. I have seen a large number of cases in Baltimore, chiefly among shipyard workers. The virulence has been much less than that reported in the West. There have been only occasional rise in temperature and little swelling of the preauricular

glands The complications of the cornea have been comparatively slight, and the spread of the infection in families has been negligible

DR JONAS S FRIEDENWALD, Baltimore I should like to add a word to the suggestion that there may be a connection between this disease and virus pneumonia In one of the hospitals in Baltimore two of the house officers made a bronchoscopic examination of a patient with virus pneumonia, after which both had a conjunctivitis in the eye used with the bronchoscope which was not bacterial and which was thought to be related to keratoconjunctivitis

DR THOMAS D ALLEN, Chicago In answer to Dr Evans' comment on the use of paredrine hydrobromide and the absence of corneal opacities in his cases, the incidence of corneal opacities varied from 15 per cent, in one epidemic, to about 80 per cent, in another

Dr Joy mentioned the unilaterality of the disease I have seen it in one eye in many cases I cannot see why it does not pass to the other eye in such patients, who are often dirty, unless there is an inherent tissue resistance

**Relation Between Bacterial Flora of the Conjunctiva and That of the Nasal Mucosa, with Special Reference to Certain Extraocular Inflammatory Diseases** DR CONRAD BERENS and EDITH L NILSON (by invitation), New York

Eighty-three bacteriologic studies were made of the conjunctival and the corresponding nasal membranes of 75 patients In vitro tests for toxicity, the results of which correlated with the results of tests on animals for pathogenicity, were used to determine individual strains of streptococci and staphylococci In 50 per cent of the cultures there was a notable relation between the nasal and the conjunctival flora; in 43.3 per cent cultures of nasal secretions yielded "toxic" organisms, with negative results for cultures of secretions from the eye, in approximately 3 per cent cultures of material from the eye yielded organisms of greater toxicity in the eye than did cultures of nasal secretions, and in only 3 per cent were the bacterial flora of the conjunctiva and those of the corresponding nasal membranes entirely unrelated

The bacteriologic relation between nasal and conjunctival infections is substantiated by unilateral clinical symptoms, and in many cases the nasal exacerbations coincide with, or are closely followed by, ocular symptoms These results suggest the advisability of examination of the nasal membranes as a possible source of infection in determining the cause of chronic and recurrent extraocular inflammatory diseases

## DISCUSSION

DR PAUL A CHANDLER, Boston I believe this report is significant It is well known that in cases of multiple boils all over the body the offending agent is nearly always present in the nose Many people who have recurrent boils and stys have been relieved by scrupulously keeping the hands away from the nose Persons who treat boils and carbuncles feel that a frequent cause of such infections on the neck is the patient's rubbing the back of the neck with the hand One would be wise to point out to patients who have recurrent stys and ocular infections the possibility that infections may be transferred from the nose to the eye

DR CONRAD BERENS, New York The mode of transference of infection is conveyance by means of the hands or the handkerchief Since these ocular infections so often occur simultaneously with infection of the nasal membranes, and since in unilateral ocular conditions the infection in the eye "lights up" with an exacerbation of the nasal infection on the same side, my associates and I are inclined to believe that infections may be transmitted by way of the nasolacrimal duct, and not merely by the hand or the handkerchief

**Written Examinations for the American Board of Ophthalmology.** DR S JUDD BEACH, Portland, Maine

The American Board of Ophthalmology has not given written examinations since 1940 It is now devising questions broad enough to reveal qualifications of the candidates, yet sufficiently rigid to obstruct concealment of their weaknesses In this report are described the development of written tests in twenty-five years of the board's existence

**Distribution of Certain Oxidative Enzymes in the Ciliary Process** DR JONAS S FRIEDENWALD, DR HEINZ HERMANN (by invitation) and DR ROBERT MOSES (by invitation), Baltimore

**Metastasis of Malignant Tumors to the Eye: Report of Two Cases** DR EDWARD C ELLETT, Memphis, Tenn

Two cases of metastatic carcinoma of the choroid are reported in which the primary lesion was in the breast The first was a case of generalized metastasis from a malignant melanoma of the abdominal wall, causing paresis of an external rectus muscle, and the second, a case of rubeosis of the iris, accompanying a malignant melanoma of the choroid

## DISCUSSION

DR ALBERT N LEMOINE, Kansas City, Mo  
In 1936 I reported a case of bilateral metastatic carcinoma of the choroid in which one eye was treated by roentgen ray therapy. Useful vision was retained for the rest of the patient's life. Recently, I had a patient who had been at the Mayo Clinic a year ago, where an exploratory operation was performed on the lung for a tumor, which proved to be an inoperable carcinoma. She was sent home for roentgen irradiation, and she has received such therapy to the chest off and on up to the present. At the time of this report the roentgenograms fail to show any growth in the lungs. Apparently, the treatment arrested the progress of the tumor. However, in January her vision began to fail, and in February it was still worse. I first saw her a month ago, when vision without correction was 6/200 in the right eye and 20/200 in the left eye, with correction it was 20/200 in the right eye and 20/100 in the left eye. In the right eye there was a large yellowish mass as described by Dr Ellett. The mass extended around the nasal part of the disk, and below and over to the macula. The highest point of elevation was 9 D. In the left eye there was a similar symmetric lesion, which was elevated about 3 D. Roentgen irradiation was immediately started. At present (I saw her three days ago) vision was correctable to 20/100 in the right eye and 20/50 in the left eye. The lesion in the left eye was completely flattened, and in the right eye it was still elevated 4 or 5 D. The visual field in the right eye was not improved. The upper quadrants were entirely obliterated, apparently the arterial circulation supplying that portion of the retina was occluded. In the left eye the visual field was almost normal. I feel it is important in such cases to use radiotherapy, especially when there is bilateral involvement.

DR C A CLAPP, Baltimore. In the July 1926 issue of the *American Journal of Ophthalmology* I reported 2 cases of so-called metastatic carcinoma of the choroid. At that time only 118 cases had been reported in the literature. I wish to show slides of 1 of the cases and to tell a bit of the later history.

The patient, aged 36, had a carcinoma of the breast removed in 1922, and her condition was considered cured. In April 1925 she consulted me because of loss of vision in the left eye. I found that she had a detachment of the retina, and, because of darkness on transillumination and the previous history, I made a diagnosis of carcinoma of the choroid. Incidentally, the roentgenograms showed involvement of the occipital bone, the spinal column and the upper ends of

both femurs. Under these circumstances, I did not advise operation for the detachment or enucleation of the eye. In July she returned with acute glaucoma in the same eye and in great pain. I therefore advised enucleation. The operation was performed on July 11. The first slide shows the growth extending over the posterior third of the eye, the next is a photomicrograph of the carcinoma which was removed from the breast, and the next shows similar carcinomatous cells from the choroid. About a month later she returned with detachment of the choroid in the other eye, which was also dark on transillumination, an indication of metastatic carcinoma in this eye. Incidentally, I believe Dr Ellett did not mention that in about one third of the reported cases the condition was bilateral.

**A Problem of Split Macula. Study of the Visual Fields.** DR JOHN N EVANS and DR E JEFFERSON BROWDER (by invitation), Brooklyn.

This article was published in full in the January 1944 issue of the *ARCHIVES*, page 431.

## DISCUSSION

DR FRANCIS HEED ADLER, Philadelphia. The authors called this tongue-shaped scotoma an angioscotoma, I am puzzled to know what vessel in the macula would give rise to an angioscotoma.

DR ALEXANDER E MACDONALD, Toronto, Canada. On account of delusions, hallucinations and emotional instability, it was necessary to remove the right cerebral cortex of a white girl aged 16 years. This was done on June 17, 1936, and on July 17 vision was 6/9 in the right eye and 6/36 in the left eye, the latter having diverged and been myopic since childhood. Dr H M Macrae reported that telescopic observations on the fixing eye showed no unsteadiness during examination of the fields and that at least 1 degree to the blind side of the hemianoptic fields of vision was preserved in each eye.

The patient made a good recovery and, after minor operations for long-standing contractures, was able to do housework and errands. Her temperament also improved.

DR JOHN N EVANS, Brooklyn. We did not mean to say that the central scotoma was an angioscotoma, although I believe part of it was. In this particular case we referred to a small "submacular" tongue and the little tongues above. They were used as controls. We could have mapped some of them farther and shown the branches. When a central scotoma is developing, with slight disturbances, such as after-images, a tongue forms along the vessels which come from the optic nerve on the side of fixation. In every instance there seems to be extra activity

on the part of the circulatory mechanism, apparently in an effort to build up, repair or reestablish the function of the central region. Our studies showed that in normal subjects the tongues of angiostoma never run more than 7 or 8 degrees from the region of fixation.

### Retinal Detachment and Trauma DR ARNOLD KNAPP New York

This article was published in full in the December 1943 issue of the ARCHIVES, page 770

#### DISCUSSION

DR MARK J SCHOENBERG, New York The first difficult point to settle is concerned with the relation of retinal detachment and trauma. It is important to consider whether the detachment develops only after direct trauma to the eyeball or whether it may appear after an indirect trauma or a "strain."

In taking the history of my patients, I have made a special effort to get minute details about any accident or unusual happening that occurred, not only immediately but weeks before the appearance of the detachment, with the intention of establishing whether the factor which produced the detachment was the sole or the precipitating cause.

Of course, most ophthalmologists would consider a direct blow on the eyeball sufficient reason for the development of a detachment, but many hesitate to believe that a long trip in a wagon or an automobile, a bump on the head, a fall, a violent jolt of the body, vibratory treatment of the scalp, prolonged reading, a miss with a golf club (the patient hitting the ground violently instead of the ball), lifting of a heavy weight, attacks of violent sneezing or coughing or straining in defecation may also be capable of bringing about such a detachment. I am glad that Dr Knapp is inclined to believe that detachment of the retina may develop after an indirect trauma. I have collected a number of instances of such indirect trauma from the histories of my own patients and I feel that often such complaints should not be brushed aside as trifling or unimportant. Indirect trauma may at times be the precipitating cause of detachment in eyes which have been predisposed by a disease preceding the trauma, such as choroiditis, cystic degeneration of the retina, degeneration of the vitreous and intraocular foreign bodies. In 9 per cent of my own patients complications of this sort have occurred. In 11 per cent the trauma was direct to the eyeball. In 45 per cent there was indirect trauma—a "strain," such as prolonged reading, sneezing or coughing. About 35 per cent of the patients gave no history of direct or indirect trauma.

The second controversial point to be discussed is the latent period which intervenes at times between direct trauma and the appearance of signs and symptoms of the detachment. I believe that in some cases the signs, and even the symptoms, of retinal detachment appear weeks, and even months, after the occurrence of the trauma. Some patients may have had vague symptoms, such as flashes or spots before the eyes, but they overlooked mentioning them to the examiner unless they were carefully questioned.

Of a number of interesting points suggested by the statistical study of retinal detachment, it is worth mentioning that 22 per cent of my patients had a low degree of myopia, of less than —1 D sph, and that 16 per cent had bilateral detachment—approximately the incidence of 14 per cent (11 per cent males and only 3 per cent females) which Dr Knapp mentioned. Further, unilateral detachment prevailed in the right eye in the males and in the left eye in the females.

DR JOHN H DUNNINGTON, New York The role of indirect trauma in the production of detachment of the retina is difficult to ascertain. I agree with Dr Knapp that this possibility cannot be ignored, but I am not in complete agreement with Dr Schoenberg, whose list of agents producing indirect trauma includes practically everything one might do, from sneezing to reading. From the standpoint of compensation, it is extremely important to make a notation on the presence or absence of trauma at the time of the initial examination. This prevents embarrassment when several weeks later the patient thinks of some vague indirect trauma he experienced several months prior to the onset of the detachment. It is my opinion that indirect trauma is of comparatively little importance in the production of detachment of the retina. As Dr Knapp has pointed out, the frequency with which both eyes are affected is a strong argument against the importance of indirect trauma.

DR JONAS S FRIEDENWALD, Baltimore I should like to comment on a minor statistical aspect of Dr Knapp's report. In discussing the frequency of detachment in respect to age, he pointed out that the age group in which detachments are most frequent is that of 40 to 60, an observation which corresponds with the experience of all commentators. The implication that detachment is less of a risk in persons over 60 is, I think, incorrect, for the proportion of persons in the community as a whole who are over 60 is steadily decreasing, and if one compares in each age group the incidence of detachment with the incidence of survival of the population as a whole, one finds that the risk of detachment steadily increases with age. The same holds with respect to the incidence of high myopia among



persons with retinal detachment. It is quite true that the most frequent record of detachment is made in cases of a medium degree of myopia, say, between 5 and 15 D. That does not imply, however, that the risk of detachment for a person with 20 to 30 D of myopia is less than that for a person with 10 D, since the frequency of the high myopia is much less. I should like, also, to comment on the long interval between injury and the onset of symptoms. No doubt the onset is often within a two week period, but there are cases, I believe, in which a much longer interval exists and in which the relation between the trauma and the detachment is at least strongly indicated. In this connection, I may report the case of a boy of 15, with hypermetropia, who was hit directly in the eye by a peach falling from a tree. He was unconscious for a minute or two. He had no visual symptoms after this accident, except during the few minutes of his recovery, until nine months later, when detachment, with an extensive disinsertion of the retina, developed. No other injury occurred during the interval, to his knowledge. Such a severe trauma, I think, cannot be disregarded as a cause of the detachment, even though the interval may be much longer than one ordinarily expects.

DR ARNOLD KNAPP, New York. In answer to the question raised by the discussers of this paper, I confess that the question of indirect trauma is a riddle and that undoubtedly the length of time before the condition develops may be long, in other words, the latent period is variable. I had hoped, however, that some one who has made a special study of ocular movements would comment on the involuntary protective movements of the eye. In what way do they take place, and under what conditions? Furthermore, can increased abdominal or thoracic pressure affect the intercerebral pressure, and in this way influence the circulation of the eye?

#### So-Called Primary Retinal Tuberculosis: Sarcoidosis of the Retina. DR ALEXANDER E. MACDONALD, Toronto, Canada

Two unusual pathologic conditions in the retina are contrasted. In the first case, isolated tubercles were observed in the detached retina of a boy aged 5 years, whose chest appeared normal on roentgenographic examination and whose reaction to the cutaneous tuberculin test was negative. In the second case, scattered nodules of sarcoidosis (Boeck's sarcoid) were noted in the retina of a woman aged 50. In both cases enucleation was done after the diagnosis of a malignant growth.

#### DISCUSSION

DR E. V. L. BROWN, Chicago. Dr MacDonald has shown in his slides something which

may be of help in differentiation of sarcoidosis and tuberculosis of the retina. In the first specimen there was a clear outline of a vesicle, or delimiting tissue, over part of the node. He pointed out an apparent separation from a central line of cells, a closing off in what might be a vessel from within a vessel. The second specimen, stained by the Verhoeff method, presented the same appearance. In the third specimen the sphincter of the iris was bent like a hook. It will be recalled that all capillaries in the iris lie behind the sphincter and that any explosive process from the capillaries would displace the sphincter in this way. In tuberculosis, on the other hand, the nodes occur at the bifurcation of veins, on the surface of the vessel. If this distinction is correct, the lesion develops inside the vessel in the case of sarcoidosis, exploding outward into the tissue in all directions, and on the surface of the vessel in the case of tuberculosis.

DR ALEXANDER E. MACDONALD, Toronto, Canada. With regard to Dr Brown's suggestion about the blood vessels, the lesions of sarcoidosis were in nearly every instance close to, but not in, the vessel.

In the last lantern slide in Dr Lloyd's case, was the lesion in the choroid or in the retina?

DR RALPH I. LLOYD, Brooklyn. It was in the retina, along one of the retinal blood vessels.

DR ALEXANDER E. MACDONALD, Toronto, Canada. Was there any caseation?

DR RALPH I. LLOYD, Brooklyn. The case was one of tuberculosis, as described by Fleischer. There was no caseation in the case, but autopsy was not performed.

#### Ophthalmoscopic Classification of Hypertensive Diseases. DR GRADY E. CLAY, and DR J. MASON BAIRD (by invitation), Atlanta, Ga.

Ophthalmology has played a significant part in the study of the various hypertensive states and is most important as a diagnostic aid. The present classification is not new, but one which has been used for years and has been found to be simple, and usually of diagnostic value for use in the medical wards.

Angiospastic hypertension is the earliest form, characterized by spasms of the arterioles. It is most common with toxemia of pregnancy and next most frequent with unilateral renal disease. The degrees of angiospasm may be estimated as grades I to IV. Ophthalmoscopically, one may grade the degree of sclerosis, and therefore the stage of essential benign hypertension. We classify arteriolar sclerosis as grades I, II, III

and IV In essential benign hypertension no changes are present except the varying degrees of sclerosis, the appearance of edema, hemorrhages and exudates, we feel, is evidence of renal damage, and we designate such a condition of the retina as secondary nephritic hypertensive neuroretinopathy Malignant hypertension, we believe, is a disease entity, characterized by severe arteriolar spasms, extreme edema and pronounced hemorrhages and exudates

The changes in the fundus seen in patients with nephritis, especially chronic glomerulonephritis with associated hypertension, are designated as primary nephritic hypertensive neuroretinopathy

#### DISCUSSION

DR P J LEINFELDER, Iowa City There is no question that the terminology in the literature is confused Graduate students at the State University of Iowa College of Medicine repeatedly come with the complaint that they cannot make head or tail out of the classification of hypertensive vascular disease As a result, my colleagues and I have had to form our own classification, which I am happy to say is in considerable agreement with Dr Clay's All may take exception to parts of his outline, yet for practical purposes it clearly expresses the state encountered in the study of large numbers of hypertensive patients

I should like to speak of the exceedingly small arterioles, the branches of the central artery of the third and fourth order Frequently the first changes are seen in these vessels and consist of local irregularities and narrowings, which may progress to such an extent that the small vessels are seen with extreme difficulty In the earliest stages the changes of hypertensive vascular disease seem to be confined exclusively to these small vessels As the disease advances, the vascular changes progress down the vessels toward the nerve head, and in the late stages they involve the largest arterioles

DR THEODORE L TERRY, Boston Section of certain sympathetic nerves and removal of functioning adenomas of the adrenal glands tend not only to control, but in some instances to cure, younger patients with severe hypertension Surgeons, cardiologists and internists most active in selecting the hypertensive patients who should have surgical treatment know of the importance of careful, detailed ophthalmic examination, and they are as concerned as the ophthalmologists over the selection and use of proper terminology They, too, should be consulted before a terminology is adopted, even though they already are guided to a great extent by the report of the ophthalmologist on the state of the fundus

DR JONAS S FRIEDENWALD, Baltimore Dr Clay has brought up an important problem in emphasizing the difficulties in nomenclature in this field It may be of help in the solution of this problem if one understands more fully how this confusion has developed Two aspects seem to me to have contributed seriously to the development of confusion in the study, knowledge and classification of vascular diseases First, vascular diseases have been classified primarily from two points of view the clinical and the pathologic, and these two systems of classification have never been satisfactorily correlated The pathologist recognizes at least two primary vascular diseases the first, a disease of the intima, which consists of proliferation of the endothelium with fatty plaques, a change which was first called arteriosclerosis and later atherosclerosis, with other new names from time to time, and the second, the hyaline degeneration of the media of the artery Since the second type occurs most often in the smaller vessels, it was originally called arteriolar sclerosis, and further names have been given it from that point of view Both these conditions may, on occasion, affect vessels of the same size, so that classification of the two diseases on the basis of the size of the vessel attacked and of the retinal disease on the fact that the arterial vessels seen there are all arterioles does not in itself resolve the confusion In some cases the major vessels in the retina may at some time show atheromatous changes and be associated with what used to be called atherosclerosis in the larger vessels of the body In other cases they may show hyaline degeneration and be associated with arteriolar sclerosis or hyaline degeneration of the media of the vessels elsewhere in the body Thus, the overlapping of these two diseases in the medium-sized vessels constitutes one of the barriers to a reasonable classification

The second aspect of the difficulty in classification is that while either of these disease processes may be primary, each may indirectly cause the other to develop For instance, if a condition begins with what used to be called arteriolar sclerosis, that is, hyaline degeneration of the media of the arterioles, hyaline degeneration of an arteriole in the vasa vasorum of a coronary artery may follow The coronary artery suffers in nutrition as a result, and an atheromatous plaque may develop on the intima of that vessel and the patient die of a myocardial infarction Thus, atherosclerosis may in many instances be secondary to the hyaline change in the small arterioles Conversely, the condition may start with what is primary atherosclerotic disease, an atheromatous plaque may form in the renal artery, and ischemia of the kidney and secondary malignant hypertension and arteriolar changes in the small vessels may develop That these two conditions are so confused in their course,



and that many patients in the terminal stage have both diseases, one primary and the other secondary, the one mutually fortifying the other, make the nomenclature confusing

DR JOHN N EVANS, Brooklyn It seems to me that the problem goes back much farther than classification. One must begin with a better understanding of the basis on which inferences are drawn. One cannot directly justify a diagnosis of "vasospasm" from anything that is seen. What one can say is, "These vessels look narrow." Then one asks, "What are the many factors which can make vessels look narrow?" One may ask the medical student, "What are the distinguishing features of choked disk and papillitis?" It is easy to tabulate over one hundred factors and conditions which can produce blurring of the nerve head. If one cannot decide what features differentiate one of these conditions from the others, how is one going to make progress in classification? If the authors' classification is to be accepted it will have to begin with acceptable criteria from which inferences may be drawn.

DR GRADY E CLAY, Atlanta, Ga We consider benign hypertension by far the most common hypertensive disease. The chances are that if in the 10 cases presented here we had examined the fundi shortly before death, we should have seen only arteriolar sclerosis, probably of grade II. The large majority of patients with hypertension show a gradual increase in the degree of arteriolar sclerosis, and that degree of sclerosis represents a grade of hypertension, in our opinion. We believe that irregularities in the caliber of the arterioles indicate that there has been a previous spasm and that the patient has had a fluctuating type of hypertension.

I did not speak of the senile type. Senile arteriosclerosis does not fit into the group of hypertensive diseases. In the patient with senile arteriosclerosis sclerosis of the arteries usually exists prior to the development of arteriolar sclerosis. The arterioles are usually straighter than those of patients of the hypertensive group, the reflex stripe is not so conspicuous, and there is not the irregularity in the caliber of the arterioles. It is our observation that chorioretinitis is especially common in cases of senile arteriosclerosis. One sees persons between the ages of 70 and 80 who have normal arterioles. The occurrence of isolated hemorrhages in cases of senile arteriosclerosis is of no prognostic value.

**Traumatic Enophthalmos** DR RAYMOND L PFEIFFER, New York

This article was published in full in the December 1943 issue of the ARCHIVES page 718

## DISCUSSION

DR JOHN ALEXANDER MACMILLAN, Montreal, Canada My associates and I have had cases of traumatic enophthalmos caused by another type of injury, namely, skiing accidents, with which Dr Pfeiffer has perhaps not come in contact. In some of these cases the floor of the orbit showed fracture, and I had felt that the enophthalmos was due to dropping of the globe into the antrum. However, a few years ago I saw a girl with enophthalmos, the result of a skiing accident, and yet no fracture of the orbit could be demonstrated roentgenographically. Dr W G M Byers was also interested in this subject at that time and took the question up with Dr Whitnall, professor of anatomy at McGill University. Dr Whitnall's explanation was that the suspensory ligament of Lockwood was probably ruptured. This ligament is formed from the sheaths of the inferior oblique and inferior rectus muscles, which join with the sheaths of the lateral and medial rectus muscles, they, in turn, are connected with the check ligaments, which are attached to the lateral and medial walls of the orbit. Since that time I have felt that rupture of this ligament is an important factor in the production of traumatic enophthalmos. In further support of this assumption, the superior maxilla may be removed and enophthalmos does not necessarily follow. I should like to know whether Dr Pfeiffer agrees.

DR PETER C KRONFELD, Chicago I wonder whether Dr Pfeiffer attaches any significance to the presence of preexisting gaps in the floor of the orbit. It is difficult to understand how an eyeball could transmit the amount of force necessary to fracture the intact floor of an orbit. Perhaps in some of these cases a congenital defect of the floor was present prior to the trauma. Such a defect could, perhaps, have been shown roentgenographically on the other side.

DR JOHN H DUNNINGTON, New York This study of Dr Pfeiffer's has interested me very much, and I wish to cite a case of mine which bears out Dr Pfeiffer's views. A girl came to me four years ago, shortly after having received a blow from a fist to her right eye. There was considerable swelling of the lids and other evidence of a severe contusion. A competent roentgenologist in New York, who specializes in sinus roentgenography, reported that there was no visible evidence of any fracture but the antrum was clouded. Within two weeks the girl had enophthalmos. I did not see her again until last week, when she returned, still complaining of diplopia and recession of the eyeball. This time a roentgenographic examination by Dr Pfeiffer revealed the type of internal fracture of the orbit he has described. Unless one is particularly careful in the interpretation in such cases, the fracture is overlooked. I agree with Dr Pfeiffer that a

fracture was demonstrable in all my cases of traumatic enophthalmos

The tremendous amount of sinking of the upper fold can be completely eliminated by simple elevation of the eye. I operated on the patient with the extreme enophthalmos which Dr Pfeiffer demonstrated. At the time of operation, simple elevation of the orbital contents from the antrum completely eliminated the sinking of the lid and the enophthalmos, I am convinced therefore that the deformity in cases of this kind is due entirely to the displacement of the tissues into the antrum. I do not mean to give the impression that this patient was permanently cured by operation, for sufficient time has not elapsed for one to judge the final result. The operative procedure used consisted of implantation of a piece of fat from the abdominal wall in the cavity created by elevation of the orbital contents. Decided improvement in the appearance was still present when the patient was last seen, two months after the operation.

DR C A CLAPP, Baltimore. Dr Pfeiffer stated that if the floor was sufficiently ruptured the eyeball might drop into the antrum, so that it would be invisible. Is this his deduction, or has he seen such a case?

DR RAYMOND L PFEIFFER, New York. The success of roentgenography in the diagnosis of ophthalmic disturbances depends on the interest of the roentgenologist in studying the bones of the face and the orbit. The fine anatomic detail of the orbit which can be brought out in carefully prepared roentgenograms is not usually appreciated by the general roentgenologist. Recently a roentgenologist wrote that it was impossible to demonstrate the floor of the orbit in roentgenograms. This statement suggests why these fractures or deformities are not usually recognized.

I do not believe that rupture of Lockwood's ligament itself is sufficient to account for enophthalmos. Rupture of the ligament probably occurs with the fracture.

In answer to Dr Kronfeld's question, I have never seen a congenital defect in the floor of the orbit in a roentgenogram. In the study of several large collections of dried skulls, I do not recall ever having seen any congenital defect or dehiscence of the floor. Whitnall mentioned hiatuses of the nasal walls.

In reply to Dr Clapp's question, I have never seen an eye completely disappear from sight as a result of injury. In the next to the last case reported, the eye nearly disappeared from view. In this case the antrum was large. Occasionally one sees very large paranasal sinuses, certainly adequate to contain an eye and all the orbital con-

tents. In the literature several cases have been recorded, von Becker and Tweedy both reported cases in which the eye disappeared from sight. In both instances the injury was produced by a cow's horn.

#### Arteritis of the Temporal Vessels: Report of a Case with Ocular Study. DR LAWRENCE T POST and DR T E SANDERS (by invitation), St Louis

Arteritis of the temporal vessels is a clinical entity, usually affecting elderly persons. It is characterized by thickening of the temporal arteries, which are painful and tender. There are also many painful areas in the scalp. It has some associated systemic symptoms, such as general malaise, fever, anorexia and anemia.

A number of cases have been reported in the general literature, in some of which ophthalmic studies were done. Except for an article from the Mayo Clinic (Johnson, R H, Harley, R D, and Horton, B I. *Am J Ophth* 26: 147 [Feb] 1943), there is no paper dealing primarily with the ocular lesions.

In the present case, a woman whose condition was one of the first reported on, about eight years ago, had a local cure at that time through surgical removal of the temporal arteries. She had no particular ocular complaints, but a peculiar lesion of the fundus was noted on routine examination.

#### Pigment Freckles of the Iris Associated with Malignant Melanoma of the Uvea. DR ALGERNON B REESE, New York

Localized accumulations of melanoblasts on the anterior surface of the iris are frequently noted in microscopic sections of eyes harboring a malignant melanoma of the uveal tract. These small multiple benign melanomas are referred to clinically as "freckles on the iris." The lesions have been interpreted as (1) coincidental, (2) implantation growths, (3) metastases, (4) extensions from the main lesion or (5) manifestations of multiple origin.

The present study indicates that the freckles are of multiple origin. In the cases reported the main lesion was in the choroid and the lesser manifestation on the iris. There occurred instances, however, in which the main lesion was in the iris and/or the ciliary body and the lesser lesion in the choroid, or in which the main lesion was in the choroid and the lesser manifestation elsewhere in the choroid. The freckles were composed of more matured cells than those comprising the main tumor and therefore were benign, with little or no power of active growth.

The clinical significance of pigment freckles on the iris lies in the fact that when they are noted in an eye in which a malignant melanoma is suspected and are not present, or are present

to a lesser degree, on the iris of the fellow eye, they offer substantiating evidence that the suspected lesion is a malignant melanoma. Also, the presence of pigment freckles on the iris seems to indicate active or malignant growth of the main lesion.

#### DISCUSSION

DR F H VERHOEFF, Boston. It would be important to determine whether the freckles antedated the tumor of the choroid. Malignant melanoma may be neurogenic, as Dr Reese mentioned, but I do not believe that Dr Georgianna Theobald has proved it to be true. In a fully developed malignant melanoma of the choroid she could easily find nerves, whatever its origin may have been. There is a possible explanation of the freckles associated with malignant melanoma not mentioned by Dr Reese. This is suggested by a frequent observation which I have made, namely, that a malignant melanoma of the corneal limbus produces an increase in the chromatophores in the tissue of the limbus for a considerable distance from the tumor. It would seem that from the tumor a substance is diffused which stimulates the chromatophores at a distance from it. In a case of a highly pigmented melanoma of the corneal limbus, with an implanted nonpigmented growth in the lower lid, I noted that the skin in a wide area around the implanted growth had become highly pigmented. This case seemed to prove that even an unpigmented malignant melanoma can stimulate the chromatophores around it.

DR THEODORE L TERRY, Boston. At birth the iris is not well developed, and the adult pigment characteristics are not evident. This change in pigmentation, or at least the appearance of pigmentation in the iris, is certainly not the development of freckles which Dr Reese describes as occurring several years later. I wonder whether he has been able to identify any such groups of cells which might be regarded as an unpigmented freckle.

Some freckles in the iris in his illustrations appear to extend deep into the stroma, perhaps involving the muscle. Has he noticed any local alteration in the motility of the iris in that region? I mention this because I have always understood this alteration of motility to be strong presumptive evidence that the lesion is a malignant melanotic neoplasm of the iris. This sign of altered motility is demonstrated graphically by use, first, of miotics and, later, of mydriatics.

It is my impression that when malignant melanoma of the choroid is well enough advanced to invade the retina, it might free tumor cells in the eye, even producing implantations in the iris. Certainly, such implantations are to be seen in cases of retinoblastoma. Thus, it is difficult to dismiss completely the evidence of the

possibility of implantation here, yet such an origin does not seem probable in the cases reported by Dr Reese. In an eye removed because of melanoma of the iris, there was a melanoma not only in the iris but in the ciliary body, some distance away there was a mass of melanoma, consisting perhaps of not more than one hundred cells, resembling closely the tumor cells of the larger melanoma of the iris. Although this mass in the ciliary body represents a metastasis, most such tumors of the iris are not extremely malignant and rarely give rise to metastases, especially within the eye itself, as melanoma of the iris appears to be related to the melanoma of the uveal tract approximately to the same degree to which the basal cell carcinoma is related to the really malignant epidermoid carcinoma. The lesion in the ciliary body may, in turn, be a secondary lesion stimulated by the primary lesion in the iris, if Dr Reese is correct in his assumption that the freckles of the iris are associated with a more posterior uveal melanoma. It was my belief that the immaturity of the cells in each region was of approximately the same grade. I shall send one of these sections to Dr Reese and see what he can make out of it.

Another point to be considered is the possible relation of this disease to melanosis oculi. At one time, Doherty pointed out that of persons who had melanosis oculi, approximately 25 per cent later showed malignant changes in the uveal tissue. The relation of freckles to malignant melanoma of the posterior uvea may indeed be similar to that of melanosis oculi to malignant uveal disease, the one being multiple and the other diffuse. One often sees a conspicuous overproduction of retinal pigment epithelium adjacent to malignant melanoma of the choroid, but heretofore this has been thought to be a result of irritation, whereas it might be related to the lesion that Dr Reese has presented.

DR ARNOLD KNAPP, New York. In confirmation of Dr Reese's statement that this condition cannot be a process of implantation on the surface of the iris, I shall mention briefly the case of a woman aged 32 who was referred to me with the diagnosis of choroiditis and glaucoma. Trephining with iridectomy had been done, and she presented the usual coloboma. The color of the iris was almost inky black. A tumor could easily be seen behind one pillar of the coloboma. The trephine opening was functioning, and the raised epithelium was studded with very small spots. The eye was removed, and microscopic examination showed that a tumor of the ciliary body had broken through at its apex and that the surface of the iris was plastered with metastatic tumors, which had also invaded the angle of the iris, the conjunctival spots were also metastases, according to Dr James Ewing.

DR ALGERNON B REESE, New York Dr Verhoeff objected to my reference to the neurogenic nature of malignant melanoma of the uvea. However, it will be recalled that I prefaced this comment by saying that I assumed that Dr Theobald's contention was correct.

Dr Verhoeff's idea that some substance may emanate from the main lesion and produce these pigment lesions elsewhere seems plausible.

The question which Dr Terry asked regarding the possible occurrence of unpigmented freckles of the iris is interesting. This possibility had occurred to me, and I intend to watch for them. In the past even the pigmented ones have been overlooked. Dr Terry asked whether benign melanoma of the iris caused any alteration in motility. I cannot answer this question specifically, but I judge that they do not, unless the lesion involves more than the anterior surface of the iris. In 1 of the cases shown the lesion involved the entire thickness of the iris and produced ectropion of the uvea. Such a lesion, I feel sure, altered the motility of the iris.

#### Pathologic Changes in the Lens Associated with Nontraumatic Iritis DR BERNARD SAMUELS, New York

This article was published in full in the January 1944 issue of the ARCHIVES, page 8.

#### Less Evident Causes of Lowered Acuity in Senile Persons DR RALPH I LLOYD, Brooklyn

It is usually possible to find in the eye of every one over 60 some cause of lowered function. Glaucoma, cataract and the vascular changes in the retinal vessels, with well known chorioretinal lesions, explain most of the beginning failures of vision in older patients. The less evident conditions may be operating on the cornea from its posterior surface or are faintly seen in the macular area as edema of the retina and choriocapillaris, or the eye may seem normal but examination of the visual fields may reveal progressive lesions, due to vascular degeneration and pressure on the optic chiasm or the optic nerve in the optic canal. This last condition has been especially studied by Fuchs and Liebrecht. Lesions in the cuneus producing hemianopsia have been better studied than the conditions first mentioned.

#### DISCUSSION

DR JONAS S FRIEDENWALD, Baltimore I disagree with Dr Lloyd in regard to a number of the interpretations he made in the early part of his paper. He spoke of deposits of fibrin on the back of the cornea in his cases. I should like to know how he knows it is fibrin.

He said the relation of endothelial dystrophy to Fuchs's dystrophy was first shown by Vogt.

It had been my impression that this relation was first called to attention by my father, at least, at the time my father published his paper, I was unable to find any reference to Vogt on that subject.

Dr Lloyd said that improvement in vision in the early stage of Fuchs's dystrophy during the day and its reduction at night are due to massage of the eyeball during the day. I believe Cogan's important contribution to the mechanism of corneal edema in Fuchs's dystrophy and the role of drying of the corneal epithelium by exposure deserve consideration.

DR RALPH I LLOYD, Brooklyn Dr Friedenwald asks how I know the fragments on the posterior surface of the cornea in the illustrations are fibrin. I do not know from my own examination, but my instruction in slit lamp study was under Koeppe, and similar deposits then seen were said to be fibrin. That the change in acuity in cases of Fuchs's dystrophy results from massage of the edematous anterior surface of the cornea during winking is my own opinion.

#### Recurring Attacks of Concomitant Exotropia, Each Followed by Transient Esotropia: Migraine the Probable Cause DR F H VERHOEFF, Boston

This article was published in full in the December 1943 issue of the ARCHIVES, page 727.

#### DISCUSSION

DR WALTER B LANCASTER, Boston The relation of accommodation and convergence is even more important than most persons realize. I shall report a case which closely resembles Dr Verhoeff's. A student nurse had difficulty in carrying on her studies. Examination showed hypermetropia of 1.25 D with a small cylinder, vision was 6/5 in each eye. Tests with the Maddox rod showed from 12 to 16 prism diopters of esophoria. It is characteristic of cases of this condition that the amount of esophoria is variable, suggestive of its dependence on a spastic condition. When she was tested with the Maddox tangent cross (the Bielschowsky method with the vertical prism to produce dissociation and a red glass before one eye to identify the image), she indicated the position of the red image, but when she was asked to give the number on the scale, she said "I cannot see the numbers." She required a — 2 or 3 D sphere to see the numbers. Obviously, she was accommodating and thus producing an esophoria which showed on the Maddox scale as 10, 12 or 16 prism diopters. With the cover test, without presentation of objects to stimulate her accommodation, simply with the light, she showed an exophoria of 6 prism diopters. Obviously, then, the underlying condition was exophoria, with the abnormal esophoria superimposed by the spasm of accom-

modation This case differed from Dr Verhoeff's in that the condition was apparent at every visit It was not a matter of periodic attacks With suitable treatment, she was able to carry on her work as a student nurse and complete her course One of my first thoughts was operation, but, fortunately, I waited long enough to satisfy myself that it was not the solution

As to how the abnormal esophoria is induced, it suffices at present to say that it is fundamentally due to the close relation between accommodation and convergence, and when the regulation of that relation breaks down, when for one cause or another the patient accommodates more than he ought, esophoria is present

Some of the patients who were treated by the Bates method come under this heading If a patient has esophoria and he can be taught to look at distant objects without accommodating, his eyes are straight, conversely, if distant objects are blurred, and he can be induced to converge his eyes, he overcomes his hypermetropia and gets clear vision, but to keep that up and have efficient sight is another matter, and failure is a source of disastrous accidents

DR THOMAS D ALLEN, Chicago Dr Verhoeff mentioned a personal, as well as a family history of migraine in his case He also noted angioneurotic edema, which is associated with migraine I wonder whether allergy may have been a cause of the migraine and the angioneurotic edema I wonder whether Dr Verhoeff has made a histamine test in this case and whether there was any notable eosinophilia

DR F H VERHOEFF, Boston Dr Lancaster's interesting comments emphasized the difficulty of measuring heterophoria but did not seem to throw any light on my case In reply to Dr Allen, I may say that the cause of the migraine was a separate problem, which I did not discuss and which, as a matter of fact, I did not solve Ergotamine was not used until the end of the last attack I planned to try histamine and, if necessary, other drugs if another series of attacks should begin

#### **Keratectomies for Treatment of Corneal Opacities** DR RAMON CASTROVIEJO, New York

This article was published in full, with discussion, in the July 1944 issue of the ARCHIVES, page 11

#### **Recession of the Trochlea** DR WENDELL L HUGHES, Hempstead, N Y

This procedure is devised to reduce the action of the superior oblique muscle when necessary The usual indications are overaction of the muscle, whether primary or secondary to paralysis or paresis of the associated inferior rectus

muscle of the opposite eye Two cases in which this procedure was performed have previously been reported The experience with 4 more cases is here presented

The technic is simple and can be carried out under local or general anesthesia

A cutaneous incision is made parallel with the orbital margin in its upper nasal position, in the region of the trochlea, nasal to the supraorbital notch The incision, 1 to 1.5 cm long, is carried down to the bone through the periosteum on the orbital rim The periosteum, which is densely adherent to the bone in the area of the trochlea, is turned backward along the roof of the orbit about 1.5 cm Two parallel incisions at right angles to the first incision are made in the periosteum to which the trochlea is attached The trochlea is easily pushed posteriorly by means of a pressure dressing The skin is closed and a small roll of gauze placed over the area of the trochlea This is held in place, the trochlea being pushed posteriorly by means of a pressure dressing In each of the 6 cases the result has been a correction of the downshoot in the nasal field, due to the overaction of the superior oblique muscle

#### **DISCUSSION**

DR WENDELL L HUGHES, Hempstead, N Y The superior oblique muscle itself is an irregularly overacting muscle in cases of this type, it is a spastic muscle, and no accurate and consistent measurements are possible The hypotropia varies with different positions of gaze, being greatest when the eye is rotated nasally and down by the action of the medial rectus and superior oblique muscles The purpose is to reduce the depressing effect of this muscle where the depressing effect of the superior oblique muscle is most marked and where the deviation of the eye is greatest

No attempt is made to put the trochlea back so many millimeters The procedure is comparable to section of the inferior oblique muscle for spasm

#### **Choice of the Fixating Eye in Paralytic and Nonparalytic Strabismus** DR JAMES W WHITE, New York

While strabismus, either paralytic or nonparalytic, may be alternating for distant and near vision, it may be seen as right or left convergent or divergent strabismus or as vertical strabismus The same eye may be the fixating eye for distant and near vision, or one eye may fixate for distance, while the fellow eye may fixate for near vision Often, when one eye fixates for both distant and near vision, fixation may change as the eyes are directed toward the six cardinal fields This choice of fixation may result in more or less variation in the amount of deviation and may,

and often does, change the treatment radically, especially in the surgical correction of the strabismus. Cases are cited.

### **Tuberous Sclerosis Report of a Case** DR ERNEST F KRUG, New York

This article was published in full in the January 1944 issue of the ARCHIVES, page 68

#### DISCUSSION

DR WALTER I LILLIE, Philadelphia The case of tuberous sclerosis presented is classic, the disease is characterized by the existence of hard tumefactions of the cerebral convolutions, formed of aggregations of a peculiar cell, related both to glial and to ganglion cells

I wish to emphasize three features of this case. First, the patient had a history of increased intracranial pressure associated with headache and choked disk, but without localizing signs of the lesion. In such a case a complete general and neurologic examination should be made as soon as possible. Second, although the roentgenograms showed evidence of increased intracranial pressure, with associated changes in the sella turcica, the visual fields did not conform with those observed with a chiasmal lesion. This in itself is a manifestation that the change in the sella turcica is only another sign of increased intracranial pressure and has no localizing value. A tumor of the third ventricle is suprasellar but does not necessarily involve the chiasm unless the optic recess of the third ventricle is involved. The third, and most important, feature of the case was the progressive loss of vision associated with choking of the disk. If vision is to be preserved, treatment should be instituted before definite signs of secondary optic nerve atrophy are visible with the ophthalmoscope. Even though the tumor cannot be located accurately, in any case of choked disk occipital decompression should be done as soon as vision is diminished, for the beginning binasal hemianopsia is positive evidence of changes in the optic nerve fibers at the disk, due to continued pressure from the edema. If the intracranial pressure is not relieved, central visual acuity will be affected. Usually there is progressive loss of vision, even though the intracranial condition is relieved later.

At present neurosurgeons are able to remove space-taking lesions in almost any portion of the brain, with an extremely low mortality rate, and the earlier this procedure can be instituted the better the end results will be.

### **Choked Disk and Low Intrathecal Pressure Associated with Tumor of the Brain** DR P J LEINFELDER, Iowa City

In a review of a number of proved cases of cerebral tumor, it was noted that under some circumstances choked disk occurred even though normal intrathecal pressure was recorded on lumbar puncture. A study of a series of 12

cases revealed that in spite of low intrathecal pressure, observation at operation or autopsy disclosed definite evidence of increased intracranial pressure. In only 2 cases was there a demonstrable block in the circulation of the cerebrospinal fluid. The records in these cases suggest that the lumbar puncture does not invariably give a true estimate of the intracranial pressure and that the choked disk is of more importance in the diagnosis of increased intracranial pressure.

#### DISCUSSION

DR ALBERT N LEMOINE, Kansas City, Mo Did Dr Leinfelder record the intraocular pressure in these cases?

DR WALTER I LILLIE, Philadelphia Dr Leinfelder's presentation brings out a point which is overlooked clinically. Many remember a paper presented before this society by Dr A J Bedell (*Papilledema Without Increased Intracranial Pressure*, *Tr Am Ophth Soc* 39: 242, 1941, *ARCH OPHTH* 27: 810 [April] 1942), in which all the cases cited were classic examples of acute optic neuritis in that precipitous loss of central visual acuity was associated with changes in the central visual fields. In Dr Leinfelder's cases choking of the disks was not accompanied by any alteration in the central visual acuity or changes in the visual field. Papilledema is a sign, not a disease entity, and is associated with many ocular syndromes. The occurrence of normal spinal fluid pressure with the presence of a proved intracranial space-taking lesion is not uncommon, and the absence of increase in spinal fluid pressure does not rule out the presence of tumor. Usually a tumor of the posterior fossa produces signs of great pressure early in the course of the syndrome, although in a certain percentage of cases there is no change in the readings of the cerebrospinal fluid pressure.

Dr Leinfelder has raised the question of the danger of examination of the spinal fluid in cases of tumor of the posterior fossa. In my experience, the risk in making such an examination has been present in cases of the supratentorial, rather than of the infratentorial, type, as the danger lies in the herniation of the cerebrum through the tentorium rather than in herniation of the medulla.

The occurrence of visual changes associated with choked disk designates a pathologic condition of the disk, due to the long-standing edema, and has no localizing value as to the position of the intracranial lesion. The occurrence of nasal contraction in the visual fields is evidence of beginning secondary optic nerve atrophy, even if pallor of the optic disk cannot be observed with the ophthalmoscope because of the edema. As soon as the binasal defect of the visual field

appears in a case with choking of the disk, the increased intracranial pressure should be relieved, even though the tumor cannot be removed, for if the pressure is allowed to continue, progressive secondary optic nerve atrophy will take place, with resulting loss of vision.

DR P J LEINFELDER, Iowa City. Dr Le-moine asked about the intraocular pressure in these cases. Unfortunately, tonometric readings were not made. However, in every case in which the patient had low intrathecal pressure and choked disk I always took the tension with

my fingers, and in no instance was the eyeball soft. I do not believe that intraocular pressure played a part in these cases.

Dr Lillie asked about the cause. The etiologic factor in each case was proved histologically, and in some instances pathologic specimens were obtained.

Herniation of the medulla after lumbar puncture has long been a subject of discussion by neurosurgeons and neurologists. I take no particular stand on the question in the presentation of this paper.



## Book Reviews

**The Romance of Medicine** By Benjamin Lee Gordon, M D Price, \$5 Pp 624, with 146 illustrations Philadelphia F A Davis Company, 1944

This is an interesting book for both the medical man and the layman, in the writing of which the author has evidently enjoyed himself to the full. From it one may learn much about "magicians, astrologers, necromancers, clairvoyants, faith healers, and fortune tellers" and of "superstitions, folklore, legend, fancies, fables, and facts"—to borrow phrases of the author. Not only are there chapters on such subjects as "early ideas of gestation and genetics," "the secret of the human automaton," "the location of the vital energy," "demonology and hysteria," "demonology and bacteriology," "astrology and medicine," "the power of mystic symbols and magical gestures," "the scapegoats of medicine" and "signature and other healing concepts," but other chapters discuss "Hebrew and Christian ideas of the after-life" and 'speculative modern concepts'. Dr Gordon also provides an excellent list of diseases which bear the names of saints.

Example after example is given of the various beliefs held among ancient peoples or savage tribes of today about the nature or causation of disease—examples drawn from all parts of the world. There are many quotations from "The Golden Bough," by Sir James Frazer, and numerous references to the literature of the Old Testament and to the Talmud. So it is a book of reference, made handy by means of a good index, but after reading the work one has to confess so many instances have been cited that they become confused in one's mind. One has often wondered how savages dared to take even one trembling step for fear that they might, in so doing, incur the wrath of the spirits which animated every object of nature about them.

Dr Gordon expresses his view thus

With regard to psychotherapy, the occult healer again anticipated the modern psychiatrist. Psychotherapy, as it will be shown, was a development of occult healing, just as bacteriology was an outgrowth of demonology, astronomy a derivative of astrology, and chemistry an amplification of alchemy.

It is sobering to think that today astrology has so many followers. Dr Gordon quotes from an article, "Health and Your Horoscope," which was published by a medical astrologer in 1940.

The author is an ophthalmologist, and his articles on the history of ophthalmology are well known. For example, "The Problem of

the Crystalline Lens" and "Oculists and Occultists" were published in the *ARCHIVES* (14:774 [No.] 1935 and 22:25 [July] 1939). Chapter 12 deals with that widespread superstition the "evil eye" and the part it has played in the lives of many people. That a visual spirit dwelt within the eye and other such ideas are also discussed. The author mentions numerous curious remedies employed in the treatment of diseases of the eye. Is one to understand from the illustration on page 67 described as an "eighth century drawing of the eyeball (from the author's collection)" that he possesses an original drawing dating from that century or does he have merely a reproduction of such a drawing?

Almost every plant and parts of almost every animal have been tried as remedies in the treatment of symptoms or in the attempt to cure disease and are being used in some part of the world today. Is it merely a case of trial and error? The book has yet to be written which traces the history of remedies of proved worth. And, in discussing any of these drugs, one must bear in mind that it is difficult to rule out faith, which is still so powerful a factor in recovery. The imponderabilia should be pondered.

The author discusses "the King's touch" in the treatment of scrofula—in fact, the subject is taken up twice (pages 249 to 250 and 358 to 359), and two paragraphs are repeated. One learns twice how Dr Samuel Johnson was "touched" by Queen Anne. This, and other errors, might well be corrected when a new edition of the work is called for.

William Withering learned the use of foxglove (*digitalis*) from an old Shropshire woman—but surely her story is overdramatized! Remedies for scurvy were in use about two hundred years before James Lind wrote of the advantages of oranges, limes and lemons, but was it not more likely "spruce beer" than a decoction of sassafras which the sailors of Jacques Cartier employed?

The book has many illustrations, but they might be much better. Many of them are merely fanciful creations of today. And why, when adequate photographs or engraved portraits could easily have been found, was it necessary to use modern redrawings of them? There are many mistakes in the spelling of proper names such as Frazier, Hyrtle, Jonathan Right, Levator, John Astruk, Finicus, Ashmoli, John of Gladdesden, St Hildegard of Bengen, Calumella Menelous and Lavarán, and 1820 should be 1880. Marlowe, not Shakespeare, was the author of "The Jew of Malta."



The keynote of the book is sounded when Dr Gordon says "Modern medicine is like a fruit tree of a well-cultivated grove or orchard whose remote origin may be traced to the wild tree of the forest"

**Blood Supply of the Visual Pathway** By Calvin M Kershner, M D, M S, in Ophthalmology Price \$3 Pp 160, with 33 illustrations Boston Meador Publishing Company, 1943

In the consideration of the structure of the visual pathways the blood supply is of great importance This monograph has gathered together in a systematic way what is known about this subject The general scheme of the blood supply to the visual pathways is first given, then each division of the pathway which has a distinctive blood supply is described in detail For convenience of discussion the visual pathway is divided into an anterior and a posterior section The anterior section comprises the orbital portion and the optic nerve up to the chiasm, the posterior section includes the rest of the visual pathway, composed of the chiasm, the tracts, the external geniculate bodies, the radiation of Grafton and the visual cortical areas in the occipital region The two parts are not strictly separate, as the blood supply of the chiasm is related to both parts After a description of the four neurons, the blood supply of the anterior section is traced from the aorta by way of the common carotid artery and its main branches, and particularly by one of the terminals, the very important ophthalmic artery The venous drainage of the orbit and the venous anastomoses come next for consideration the facial vein, the pterygoid plexus and the intracranial sinuses The blood for the posterior portion comes from the internal carotid and the vertebral arteries, and the venous drainage is the same as that of the midbrain and the posterior cortical area, where the blood finally enters the sinuses of the dura mater The second, and most important, part

of the book takes up (a) the retinal elements with a detailed description of the retinal and choroidal circulation, (b) the optic nerve, and (c) the lateral geniculate body, the optic radiations and the cortex—the area striata In this section the relation of the blood supply to clinical and pathologic conditions is also mentioned and their importance in the understanding of clinical symptoms demonstrated The text is clearly written, and the subject matter is illustrated by simple drawings in black and white, taken from recognized authorities The book concludes with a complete bibliography

The author has succeeded, with commendable industry, in providing a valuable monograph which contains in a relatively small space much important, and often not very accessible, information, which will be found useful by the ophthalmologist and the neurologist

ARNOLD KNAPP

**Minor Surgery** Edited by Humphry Rolleston and Alan Moncrieff Price, \$5 Pp 174 New York Philosophical Library, Inc, 1943

The subject of minor surgery is treated in 18 chapters and covers practically all minor surgical conditions, such as minor wounds, sprains, disabilities of the feet and hands, and minor disturbances of the nose and throat, ear, eye, skin and genitourinary system, and anesthesia These chapters are written by prominent English surgeons The subject matter is covered in 155 pages, with an index of 18 pages

The chapter on the eye is written by J S Arkle, ophthalmic surgeon to the Royal Victoria Infirmary, Newcastle-upon-Tyne In this chapter the following subjects are discussed removal of foreign bodies, mild infections, such as styes, cysts, dacryocystitis, repair of laceration of the lids, and treatment of burns of the eye In the small space (6 pages) that this chapter occupies, only a superficial description of the procedures can, of course, be given

ARNOLD KNAPP

# Directory of Ophthalmologic Societies \*

## INTERNATIONAL

### INTERNATIONAL ASSOCIATION FOR PREVENTION OF BLINDNESS

President Dr P Baillart, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France  
Secretary-General Prof M Van Duyse, Universite de Gand, Gand, Prov Ostflandern, Belgium  
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France

### INTERNATIONAL OPHTHALMOLOGIC CONGRESS

President Prof Nordenson, Serafimerlasarettet, Stockholm, Sweden  
Secretary Dr Ehlers, Jerbanenegade 41, Copenhagen, Denmark

### INTERNATIONAL ORGANIZATION AGAINST TRACHOMA

President Dr A F MacCallan, 17 Horseferry Rd, London, England

### PAN-AMERICAN CONGRESS OF OPHTHALMOLOGY

President Dr Harry S Gradle, 58 E Washington St, Chicago  
Executive Secretaries Dr Conrad Berens, 35 E 70th St, New York Dr M E Alvaro, 1511 Rua Consolacão, São Paulo, Brazil

## FOREIGN

### ALL-INDIA OPHTHALMOLOGICAL SOCIETY

President Dr B K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore  
Secretary Dr G Zachariah, Flitcham, Marshall's Rd, Madras

### BRITISH MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President Dr W Clark Souter, 9 Albyn Pl, Aberdeen, Scotland  
Secretary Dr Frederick Ridley, 12 Wimpole St, London, W 1

### CHENG TU OPHTHALMOLOGICAL SOCIETY

President Dr Eugene Chan  
Secretary Dr K S Sun  
Place Eye, Ear, Nose and Throat Hospital, Chengtu, China

### CHINESE OPHTHALMOLOGY SOCIETY

President Dr C H Chou, 363 Avenue Haig, Shanghai  
Secretary Dr F S Tsang, 221 Foochow Rd, Shanghai

### CHINESE OPHTHALMOLOGICAL SOCIETY OF PEIPING

President Dr H T Pi, Peiping Union Medical College, Peiping  
Secretary Dr C K Lin, 180 Hsi-Lo-yen Chienmeng, Peiping  
Place Peiping Union Medical College, Peiping Time Last Friday of each month

### GERMAN OPHTHALMOLOGICAL SOCIETY

President Prof W Lohlein, Berlin  
Secretary Prof E Engelking, Heidelberg

### HUNGARIAN OPHTHALMOLOGICAL SOCIETY

President Prof I Imre, Budapest  
Assistant Secretary Dr Stephen de Grosz, University Eye Hospital, Máriautca 39, Budapest  
All correspondence should be addressed to the Assistant Secretary

### MIDLAND OPHTHALMOLOGICAL SOCIETY

President Dr W Niccol, 4 College Green, Gloucester, England  
Secretary Mr T Harrison Butler, 61 Newhall St, Birmingham 3, England  
Place Birmingham and Midland Eye Hospital

### NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President Dr A MacRae, 6 Jesmond Rd, Newcastle-upon-Tyne, England  
Secretary Dr Percival J Hay, 350 Glossop Rd, Sheffield 10, England  
Place Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation Time October to April

### OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President Dr A James Flynn, 135 Macquarie St, Sydney  
Secretary Dr D Williams, 193 Macquarie St, Sydney

### OPHTHALMOLOGICAL SOCIETY OF EGYPT

President Prof Dr Mohammed Mahfouz Bey, Government Hospital, Alexandria  
Secretary Dr Mohammed Khalil, 4 Baehler St, Cairo  
All correspondence should be addressed to the secretary, Dr Mohammed Khalil

### OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President Mr Charles B Goulden, OBE, MD, MCh, 89 Harley St, London, England  
Secretary Mr Frank W Law, MA, MD, FRCS, 30 Devonshire Pl, London W 1, England

### OPHTHALMOLOGY SOCIETY OF BOMBAY

President Dr D D Sathaye, 127 Girgaum Rd, Bombay 4, India  
Secretary Dr H D Dastur, Dadar, Bombay 14, India  
Place H B A Free Ophthalmic Hospital, Parel, Bombay 12 Time First Friday of every month

### OXFORD OPHTHALMOLOGICAL CONGRESS

Master Mr P G Doyne, 60 Queen Anne St, London, W 1, England  
Secretary-Treasurer Dr F A Anderson, 12 St John's Hill, Shrewsbury, England  
Place Oxford, England Time July 8-9, 1943

### PALESTINE OPHTHALMOLOGICAL SOCIETY

President Dr Arich Feigenbaum, Abyssinian St 15, Jerusalem  
Secretary Dr E Sinai, Tel Aviv

### POLISH OPHTHALMOLOGICAL SOCIETY

President Dr W Kapuściński, 2 Waly Batorego, Poznan  
Secretary Dr J Sobański, Lindley'a 4, Warsaw  
Place Lindley'a 4 Warsaw

\* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date

ROYAL SOCIETY OF MEDICINE, SECTION OF  
OPHTHALMOLOGY

President Col F A Juler, 96 Harley St, London,  
W 1, England  
Secretary Dr Harold Ridley, 60 Queen Anne St,  
London, W 1, England

SÃO PAULO SOCIETY OF OPHTHALMOLOGY

President Dr W Belfort Mattos, Caixa Postal, 4086,  
São Paulo, Brazil  
Secretary Dr Silvio de Almeida Toledo, Enfermaria  
Santa Luzia, Santa Casa de Misericórdia, Cesario  
Motta, St 112, São Paulo, Brazil

SOCIEDAD ARGENTINA DE OFTALMOLOGIA

Chairman Dr Jorge Malbrán, Buenos Aires  
Secretary Dr Benito Just Tiscornia, Santa Fe 1171,  
Buenos Aires

SOCIEDAD OFTALMOLOGIA DEL LITORAL,  
ROSARIO (ARGENTINA)

President Prof Dr Carlos Weskamp, Laprida 1159,  
Rosario  
Secretary Dr Juan M Vila Ortiz, Cordoba 1433,  
Rosario  
Place Rosario Time Last Saturday of every month,  
April to November, inclusive All correspondence  
should be addressed to the President

SOCIEDADE DE OPHTHALMOLOGIA E OTO-RHINO-  
LARYNGOLOGIA DA BAHIA

President Dr Theonilo Amorim, Barra Avenida,  
Bahia, Brazil  
Secretary Dr Adroaldo de Alencar, Brazil  
All correspondence should be addressed to the President

SOCIETA OFTALMOLOGICA ITALIANA

President Prof Dott Giuseppe Ovio, Ophthalmological  
Clinic, University of Rome, Rome  
Secretary Prof Dott Epimaco Leonardi, Via del  
Gianicolo, 1, Rome

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary Dr René Onfray, 6 Avenue de la Motte  
Picquet, Paris, 7<sup>e</sup>

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President Prof K G Ploman, Stockholm  
Secretary Dr K O Granstrom, Sodermalmstorg 4  
III tr, Stockholm, So

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President Dr D Arieh-Friedman, 96 Allenby St, Tel  
Aviv, Palestine.  
Secretary Dr Sadger Max, 9 Bialik St, Tel Aviv,  
Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC  
ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman Dr Frederick C Cordes, 384 Post St, San  
Francisco  
Secretary Dr R J Masters, 23 E Ohio St, Indian-  
apolis

AMERICAN ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President Dr Lawrence T Post, Metropolitan Bldg,  
St Louis  
President-Elect Dr Gordon B New, Mayo Clinic,  
Rochester, Minn  
Executive Secretary-Treasurer Dr William L Bene-  
dict, 101-1st Ave Bldg, Rochester, Minn

AMERICAN OPHTHALMOLOGICAL SOCIETY

President Dr S Judd Beach, 704 Congress St, Port-  
land, Maine  
Secretary-Treasurer Dr Walter S Atkinson, 129  
Clinton St, Watertown, N Y

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC

Chairman Dr Frederick C Cordes, 384 Post St, San  
Francisco  
Secretary-Treasurer Major Brittain F Payne, School  
of Aviation Medicine, Randolph Field, Texas

CANADIAN MEDICAL ASSOCIATION, SECTION ON  
OPHTHALMOLOGY

President Dr Alexander E MacDonald, 170 St George  
St, Toronto  
Secretary-Treasurer Dr L J Sebert, 170 St George  
St, Toronto

CANADIAN OPHTHALMOLOGICAL SOCIETY

President Dr R Evatt Mathers, 34½ Morris St,  
Halifax, N S  
Secretary-Treasurer Dr Kenneth B Johnston, Suite 1,  
1509 Sherbrooke St W, Montreal

NATIONAL SOCIETY FOR THE PREVENTION OF  
BLINDNESS

President Mr Mason H Bigelow, 1790 Broadway,  
New York  
Secretary Miss Regina E Schneider, 1790 Broadway,  
New York  
Executive Director Mrs Eleanor Brown Merrill, 1790  
Broadway, New York

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY,  
SECTION ON EYE, EAR, NOSE AND THROAT

President Dr N Zwaifler, 46 Wilbur Ave, Newark  
Secretary Dr William F Keim Jr, 25 Roseville Ave,  
Newark  
Place 91 Lincoln Park South, Newark Time 8 45  
p m, second Monday of each month, October to May

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr L J Friend, 425 E Grand Ave, Beloit,  
Wis  
Secretary Dr G L McCormick, 626 S Central Ave,  
Marshfield

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President Dr Paul A Chandler, 5 Bay State Rd,  
Boston  
Secretary-Treasurer Dr Merrill J King, 264 Beacon  
St, Boston  
Place Massachusetts Eye and Ear Infirmary, 243  
Charles St, Boston Time 8 p m, third Tuesday of  
each month from November to April, inclusive

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President Dr D H O'Rourke, 1612 Tremont Pl,  
Denver  
Secretary-Treasurer Dr C Allen Dickey, 450 Sutter  
St, San Francisco

PUGET SOUND ACADEMY OF OPHTHALMOLOGY  
AND OTO-LARYNGOLOGY

President Dr L L Bull, 1215-14th Ave, Seattle,  
Wash  
Secretary-Treasurer Dr Barton E Peden, 301 Stimson  
Bldg, Seattle 1  
Place Seattle or Tacoma, Wash Time Third Tues-  
day of each month except June, July and August

ROCK RIVER VALLEY EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr J Sheldon Clark, 27 E Stephenson St,  
Freeport, Ill  
Secretary-Treasurer Dr Harry R Warner, 321 W  
State St, Rockford, Ill  
Place Rockford, Ill, or Janesville or Beloit, Wis  
Time Third Tuesday of each month from October  
to April, inclusive

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr M H Pike, Midland, Mich  
Secretary-Treasurer Dr H H Heuser, 207 Davidson  
Bldg, Bay City, Mich  
Place Saginaw or Bay City, Mich Time Second  
Tuesday of each month, except July, August and  
September

SIoux VALLEY EYE AND EAR ACADEMY

President Dr J C Decker, 515 Francis Bldg, Sioux  
City, Iowa  
Secretary-Treasurer Dr J E Dvorak, 408 Davidson  
Bldg, Sioux City, Iowa

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE,  
EAR, NOSE AND THROAT

Chairman Dr John H Burleson, 414 Navarro St,  
San Antonio, Texas  
Secretary Dr J W Jervey Jr, 101 Church St,  
Greenville, S C

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE  
AND THROAT

President Dr H L Brehmer, 221 W Central Ave,  
Albuquerque, N Mex  
Secretary Dr A E Cruthirds, 1011 Professional Bldg,  
Phoenix, Ariz

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President Dr W M Dodge, 716 First National Bank  
Bldg, Battle Creek  
Secretary-Treasurer Dr Kenneth Lowe, 25 W Mich-  
igan Ave, Battle Creek  
Time Last Thursday of September, October, Novem-  
ber, March, April and May

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr Ray Parker, 218 Franklin St, Johnston,  
Pa  
Secretary-Treasurer Dr J McClure Tyson, Deposit  
Nat'l Bank Bldg, DuBois

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR,  
NOSE AND THROAT SECTION

President Dr Raymond C Cook, 701 Main St, Little  
Rock  
Secretary Dr K W Cosgrove, Urquhart Bldg, Little  
Rock

COLORADO OPHTHALMOLOGICAL SOCIETY

President Dr C A Ringle, 912-9th Ave, Greeley  
Secretary Dr W A Ohmart, 1102 Republic Bldg,  
Denver  
Place University Club, Denver Time 7 30 p m,  
third Saturday of each month, October to May, in-  
clusive

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON  
EYE, EAR, NOSE AND THROAT

President Dr F L Phillips, 405 Temple St, New  
Haven  
Secretary-Treasurer Dr W H Turnley, 1 Atlantic  
St, Stamford, Conn

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President William O Martin Jr, Doctors Bldg,  
Atlanta  
Secretary-Treasurer Dr C K McLaughlin, 526  
Walton St, Macon

INDIANA ACADEMY OF OPHTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr F McK Ruby, Union City  
Secretary Dr Edwin W Dyar Jr, 23 E Ohio St,  
Indianapolis  
Place French Lick Time First Wednesday in April

IOWA ACADEMY OF OPHTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr J K Von Lackum, 117-3d St S E,  
Cedar Rapids  
Secretary-Treasurer Dr B M Merkel, 604 Locust St,  
Des Moines

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND  
OTOLARYNGOLOGICAL SOCIETY

President Dr Val H Fuchs, 200 Carondelet St, New  
Orleans  
Secretary-Treasurer Dr Edley H Jones, 1301 Wash-  
ington St, Vicksburg, Miss

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF  
OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr Robert H Fraser, 25 W Michigan  
Ave, Battle Creek  
Secretary Dr R G Laird, 114 Fulton St, Grand  
Rapids

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr George E McGeary, 920 Medical Arts  
Bldg, Minneapolis  
Secretary Dr William A Kennedy, 372 St Peter St,  
St Paul  
Time Second Friday of each month from October to  
May

## MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President Dr William Morrison, 208 N Broadway,  
Billings, Mont  
Secretary Dr Fritz D Hurd, 309 Medical Arts Bldg,  
Great Falls

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr W Howard Morrison, 1500 Medical  
Arts Bldg, Omaha  
Secretary-Treasurer Dr John Peterson, 1307 N St  
Lincoln

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON  
OPHTHALMOLOGY, OTOTOLOGY AND  
RHINOLARYNGOLOGY

Chairman Dr B E Failing, 31 Lincoln Park, Newark  
Secretary Dr George Meyer, 410 Haddon Ave,  
Camden

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR,  
NOSE AND THROAT SECTION

Chairman Dr Harold J Joy, 504 State Tower Bldg,  
Syracuse 2  
Secretary Dr Maxwell D Ryan, 660 Madison Ave,  
New York 21

NORTH CAROLINA EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr Hugh C Wolfe, 102 N Elm St,  
Greensboro  
Secretary Dr Vanderbilt F Couch, 104 W 4th St,  
Winston-Salem

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY  
AND OTO-LARYNGOLOGY

President Dr W L Diven, City National Bank Bldg,  
Bismarck  
Secretary-Treasurer Dr A E Spear, 20 W Villard,  
Dickenson

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr J L Sanders, 222 N Main St, Green-  
ville  
Secretary Dr J H Stokes, 125 W Cheves St,  
Florence

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr Wesley Wilkerson, 700 Church St,  
Nashville  
Secretary-Treasurer Dr W D Stinson, 124 Physicians  
and Surgeons Bldg, Memphis

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL  
SOCIETY

President Dr F H Rosebrough, 603 Navarro St,  
San Antonio  
Secretary Dr M K McCullough, 1717 Pacific Ave,  
Dallas

## UTAH OPHTHALMOLOGICAL SOCIETY

President Dr R B Maw, 699 E South Temple, Salt  
Lake City  
Secretary-Treasurer Dr Charles Ruggeri Jr, 1120  
Boston Bldg, Salt Lake City  
Place University Club, Salt Lake City Time 7 00  
p m, third Monday of each month

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND  
OPHTHALMOLOGY

President Dr Mortimer H Williams, 30½ Franklin  
Rd S W, Roanoke  
Secretary-Treasurer Dr Meade Edmunds, 34 Franklin  
St, Petersburg

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE,  
EAR, NOSE AND THROAT SECTION

President Dr George Traugh, 309 Cleveland Ave,  
Fairmont  
Secretary Dr Welch England, 621½ Market St,  
Parkersburg

## LOCAL

## OTO-LARYNGOLOGY

President Dr Paul Neely, 1020 S W Taylor St,  
Portland  
Secretary-Treasurer Dr Lewis Jordon, 1020 S W  
Taylor St, Portland  
Place Good Samaritan Hospital, Portland Time  
Third Tuesday of each month

PENNSYLVANIA ACADEMY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr Lewis T Buckman, 83 S Franklin St,  
Wilkes-Barre  
Secretary Pro Tem Dr Paul C Craig, 232 N 5th  
St, Reading  
Time Last week in April

RHODE ISLAND OPHTHALMOLOGICAL AND  
OTOLOGICAL SOCIETY

Acting President Dr N Darrell Harvey, 112 Water-  
man St, Providence.  
Secretary-Treasurer Dr Linley C Happ, 124 Water-  
man St, Providence  
Place Rhode Island Medical Society Library, Provi-  
dence Time 8 30 p m, second Thursday in  
October, December, February and April

AKRON ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr E L Mather, 39 S Main St, Akron,  
Ohio  
Secretary-Treasurer Dr V C Malloy, 2d National  
Bank Bldg, Akron, Ohio  
Time First Monday in January, March, May and  
November

## ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr B M Cline, 153 Peachtree St N E,  
Atlanta, Ga  
Acting Secretary Dr A V Hallum, 478 Peachtree  
St N E, Atlanta, Ga  
Place Grady Hospital Time 6 00 p m, fourth Mon-  
day of each month, from October to May

BALTIMORE MEDICAL SOCIETY, SECTION ON  
OPHTHALMOLOGY

Chairman Dr Ernst Bodenheimer, 1212 Eutaw Pl,  
Baltimore  
Secretary Dr Thomas R O'Rourke, 104 W Madison  
St, Baltimore  
Place Medical and Chirurgical Faculty, 1211 Cathedral  
St Time 8 30 p m, fourth Thursday of each  
month from October to March

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President Each member, in alphabetical order  
 Secretary Dr Luther E Wilson, 919 Woodward Bldg, Birmingham, Ala  
 Place Tutwiler Hotel Time 6 30 p m, second Tuesday of each month, September to May, inclusive

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President Dr William B Agan, 1 Nevins St, Brooklyn  
 Secretary-Treasurer Dr Benjamin C Rosenthal, 140 New York Ave, Brooklyn  
 Place Kings County Medical Society Bldg, 1313 Bedford Ave Time Third Thursday in February, April, May, October and December

BUFFALO OPHTHALMOLOGIC CLUB

President Dr Walter F King, 519 Delaware Ave, Buffalo  
 Secretary-Treasurer Dr Sheldon B Freeman, 196 Linwood Ave, Buffalo  
 Time Second Thursday of each month

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Each member, in alphabetical order  
 Secretary Dr Douglas Chamberlain, Chattanooga Bank Bldg, Chattanooga, Tenn  
 Place Mountain City Club Time Second Thursday of each month from September to May

CHICAGO OPHTHALMOLOGICAL SOCIETY

President Dr Vernon M Leech, 55 E Washington St, Chicago  
 Secretary Dr W A Mann, 30 N Michigan Ave, Chicago  
 Place Chicago Towers Club, 505 N Michigan Ave  
 Time Third Monday of each month from October to May

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY STAFF

Chairman Dr D T Vail, 441 Vine St, Cincinnati  
 Secretary Dr A A Levin, 441 Vine St, Cincinnati  
 Place Cincinnati General Hospital Time 7 45 p m, third Friday of each month except June, July and August

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman Dr Shandor Monson, 1621 Euclid Ave, Cleveland  
 Secretary Dr Carl Ellenberger, 14805 Detroit Ave, Cleveland  
 Time Second Tuesday in October, December, February and April

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman Dr W S Reese, 1901 Walnut St, Philadelphia  
 Clerk Dr George F J Kelly, 37 S 20th St, Philadelphia  
 Time Third Thursday of every month from October to April, inclusive

COLUMBUS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

Chairman Dr H D Emswiler, 370 E Town St, Columbus, Ohio  
 Secretary-Treasurer Dr D G Sanor, 206 E State St, Columbus, Ohio  
 Place The Neil House Time 6 p m, first Monday of each month

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr Arthur Padillo, 414 Medical Professional Bldg, Corpus Christi, Texas  
 Secretary Dr Edgar G Mathis, 815 Medical Arts Bldg, Corpus Christi, Texas  
 Time Second Friday of each month from October to May

DALLAS ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Ruby K Daniel, Medical Arts Bldg, Dallas 1, Texas  
 Secretary Dr Tom Barr, Medical Arts Bldg, Dallas 1, Texas  
 Place Dallas Athletic Club Time 6 30 p m, first Tuesday of each month from October to June The November, January and March meetings are devoted to clinical work

DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr H C Schmitz, 604 Locust St, Des Moines, Iowa  
 Secretary-Treasurer Dr Byron M Merkel, 604 Locust St, Des Moines, Iowa  
 Time 7 45 p m, third Monday of every month from September to May

DETROIT OPHTHALMOLOGICAL CLUB

Chairman Dr Raymond S Goux, 545 David Whitney Bldg, Detroit 26  
 Secretary Dr Arthur Hale, 1609 Eaton Tower, Detroit  
 Place Club rooms of Wayne County Medical Society  
 Time 6 30 p m, third Thursday of each month, November through April

DETROIT OPHTHALMOLOGICAL SOCIETY

President Dr Parker Heath, 1553 Woodward Ave, Detroit  
 Secretary Dr Leland F Carter, 1553 Woodward Ave, Detroit  
 Place Club rooms of Wayne County Medical Society  
 Time Third Thursday of each month from November to April, inclusive

EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President Appointed at each meeting  
 Secretary-Treasurer Dr Joseph L Holohan, 330 State St, Albany  
 Time Third Wednesday in October, November, March, April, May and June

FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Rex Howard, 602 W 10th St, Fort Worth, Texas  
 Secretary-Treasurer Dr R H Gough, Medical Arts Bldg, Fort Worth, Texas  
 Place Medical Hall, Medical Arts Bldg Time 7 30 p m, first Friday of each month except July and August

# HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SECTION

President Dr Lyle J Logue, 1304 Walker Ave, Houston, Texas  
 Secretary Dr John T Stough, 803 Medical Arts Bldg, Houston, Texas  
 Place Medical Arts Bldg, Harris County Medical Society Rooms Time 8 p m, second Thursday of each month from September to June

# INDIANAPOLIS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President Dr Myron Harding, 23 E Ohio St, Indianapolis  
 Secretary Dr Kenneth L Craft, 23 E Ohio St, Indianapolis  
 Place Indianapolis Athletic Club Time 6 30 p m, second Thursday of each month from November to May

# KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Edgar Johnson, 906 Grand Ave, Kansas City, Mo  
 Secretary Dr W E Keith, 1103 Grand Ave, Kansas City, Mo  
 Time Third Thursday of each month from October to June The November, January and March meetings are devoted to clinical work

# LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr Harold Snow, 614 S Pacific Ave, San Pedro, Calif  
 Secretary-Treasurer Dr Oliver R Nees, 508 Times Bldg, Long Beach, Calif  
 Place Professional Bldg Time Last Wednesday of each month from October to May

# LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr M E Trainor, 523 W 6th St, Los Angeles  
 Secretary-Treasurer Dr Orrie E Ghrist, 210 N Central Ave, Glendale, Calif  
 Place Los Angeles County Medical Association Bldg, 1925 Wilshire Blvd Time 6 00 p m, fourth Monday of each month from September to May, inclusive

# LOUISVILLE EYE AND EAR SOCIETY

President Dr Joseph S Heitger, Heyburn Bldg, Louisville, Ky  
 Secretary-Treasurer Dr J W Fish, 321 W Broadway, Louisville, Ky  
 Place Brown Hotel Time 6 30 p m, second Thursday of each month from September to May, inclusive

# LOWER ANTHRACITE EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Each member in alphabetical order  
 Secretary Dr James J Monohan 31 S Jardin St, Shenandoah, Pa

# MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr P S Constantinople, 1835 I St N W, Washington  
 Secretary Dr Frazier Williams, 1801 I St N W, Washington  
 Place 1718 M St N W Time 8 p m, third Friday of each month from October to April, inclusive

# MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Each member in alphabetical order  
 Secretary Dr Sam H Sanders, 1089 Madison Ave, Memphis, Tenn  
 Place Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital Time 8 p m, second Tuesday of each month from September to May

# MILWAUKEE OTO-OPHTHALMIC SOCIETY

President Dr Edwin C Bach, 324 E Wisconsin Ave, Milwaukee  
 Secretary-Treasurer Dr Ralph T Rank, 238 W Wisconsin Ave, Milwaukee  
 Place University Club Time 6 30 p m, second Tuesday of each month

# MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman Dr H V Dutrow, 1040 Fidelity Medical Bldg, Dayton, Ohio  
 Secretary-Treasurer Dr Maitland D Place, 981 Reibold Bldg, Dayton, Ohio  
 Place Van Cleve Hotel Time 6 30 p m, first Tuesday of each month from October to June, inclusive

# MONTREAL OPHTHALMOLOGICAL SOCIETY

President Dr J Rosenbaum, 1396 Ste Catherine St W, Montreal, Canada  
 Secretary Dr L Tessier, 1230 St Joseph Blvd E, Montreal, Canada  
 Time Second Thursday of October, December, February and April

# NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr M M Cullom, 700 Church St, Nashville, Tenn  
 Secretary Dr R E Sullivan, 432 Doctors Bldg, Nashville, Tenn  
 Place St Thomas Hospital Time 8 p m, third Monday of each month from October to May

# NEW HAVEN OPHTHALMOLOGICAL SOCIETY

President Dr William H Ryder, 185 Church St, New Haven, Conn  
 Secretary Dr Frederick A Wiess, 255 Bradley St, New Haven, Conn

# NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr W B Clark, 1012 American Bank Bldg, New Orleans  
 Secretary Dr Mercer G Lynch, 1018 Maison Blanche Bldg, New Orleans  
 Place Louisiana State University Medical Bldg Time 8 p m, second Tuesday of each month from October to May

NEW YORK ACADEMY OF MEDICINE, SECTION OF  
OPHTHALMOLOGY

Chairman Dr Frank C Keil, 660 Madison Ave, New York  
Secretary Dr Willis S Knighton, 121 E 61st St, New York  
Time 8 30 p m, third Monday of every month from October to May, inclusive

NEW YORK SOCIETY FOR CLINICAL  
OPHTHALMOLOGY

President Dr Milton Berliner, 57 W 57th St, New York  
Secretary Dr Benjamin Esterman, 983 Park Ave, New York  
Place Squibb Hall, 745-5th Ave Time 8 p m, first Monday of each month from October to May, inclusive

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr James P Luton, 117 N Broadway, Oklahoma City  
Secretary Dr Harvey O Randel, 117 N Broadway, Oklahoma City  
Place University Hospital Time Second Tuesday of each month from September to May

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL  
AND OTO-LARYNGOLOGICAL SOCIETY

President Dr D D Stonecypher, Nebraska City, Neb  
Secretary-Treasurer Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha  
Place Omaha Club, 20th and Douglas Sts, Omaha  
Time 6 p m dinner, 7 p m program, third Wednesday of each month from October to May

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President Dr Thomas Sanfacon, 340 Park Ave, Paterson, N J  
Secretary-Treasurer Dr J Averbach, 435 Clinton Ave, Clinton, N J  
Place Paterson Eye and Ear Infirmary Time 9 p m, last Friday of every month, except June, July and August

PHILADELPHIA COUNTY MEDICAL SOCIETY,  
EYE SECTION

President Dr Isaac Tassman, 136 S 16th St, Philadelphia  
Secretary Dr Glen Gregory Gibson, 255 S 17th St, Philadelphia  
Time First Thursday of each month from October to May

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President Dr George H Shuman, 351-5th Ave, Pittsburgh  
Secretary Dr Robert J Billings, 509 Liberty Ave, Pittsburgh  
Place Pittsburgh Academy of Medicine Bldg Time Fourth Monday of each month, except June, July, August and September

READING EYE, EAR, NOSE AND THROAT SOCIETY

President Dr R M Brickbauer, Shillington, Pa  
Secretary Dr Paul C Craig, 232 N 5th St, Reading, Pa  
Place Wyomissing Club Time 6 30 p m, third Wednesday of each month from October to July

RICHMOND OPHTHALMOLOGICAL AND OTO-  
LARYNGOLOGICAL SOCIETY

President Dr Peter N Pastore, Medical College of Virginia, Richmond, Va  
Secretary Dr Clifford A Folkes, Professional Bldg, Richmond, Va  
Place Westmoreland Club Time 6 p m, second Monday of each month from October to May

ROCHESTER EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr Frank Barber, 75 S Fitzhugh St, Rochester, N Y  
Secretary-Treasurer Dr Charles T Sullivan, 277 Alexander St, Rochester, N Y

ST LOUIS OPHTHALMIC SOCIETY

President Dr C C Beisbarth, 3720 Washington Blvd, St Louis  
Secretary Dr H R Hildreth, 508 N Grand Blvd, St Louis  
Place Oscar Johnson Institute Time Clinical meeting, 5 30 p m, dinner and scientific meeting 6 30 p m, fourth Friday of each month from October to April, inclusive, except December

SAN ANTONIO OPHTHALMO-OTO-LARYNGOLOGICAL  
SOCIETY

President Dr Belvin Pritchett, 705 E Houston St, San Antonio 5, Texas  
Secretary-Treasurer Lt Col John L Matthews, AAF School of Aviation Medicine, Randolph Field, Texas  
Place San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center  
Time 7 p m, second Tuesday of each month from October to May

SAN FRANCISCO COUNTY MEDICAL SOCIETY,  
SECTION ON EYE, EAR, NOSE AND THROAT

Chairman Dr Roy H Parkinson, 870 Market St, San Francisco  
Secretary Dr A G Rawlins, 384 Post St, San Francisco  
Place Society's Bldg, 2180 Washington St, San Francisco Time Fourth Tuesday of every month except June, July and December

SHREVEPORT EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr David C Swearingen, Slattery Bldg, Shreveport, La  
Secretary-Treasurer Dr Kenneth Jones, Medical Arts Bldg, Shreveport, La  
Place Shreveport Charity Hospital Time 7 30 p m, first Monday of every month except July, August and September



SPokane ACADEMY OF OPHTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr Clarence A Veasey Sr, 421 W River-  
side Ave, Spokane, Wash  
Secretary Dr Clarence A Veasey Jr, 421 W River-  
side Ave, Spokane, Wash  
Place Spokane Medical Library Time 8 p m, fourth  
Tuesday of each month except June, July and August

SYRACUSE EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr A H Rubenstein, 713 E Genesee St,  
Syracuse, N Y  
Secretary-Treasurer Dr I H Blaisdell, 713 E  
Genesee St, Syracuse, N Y  
Place University Club Time First Tuesday of each  
month except June, July and August

TOLEDO EYE, EAR, NOSE AND  
THROAT SOCIETY

Chairman Dr E W Campbell, 316 Michigan St,  
Toledo, Ohio  
Secretary Dr L C Ravin, 316 Michigan St, Toledo,  
Ohio  
Place Toledo Club Time Each month except June,  
July and August

TORONTO ACADEMY OF MEDICINE, SECTION OF  
OPHTHALMOLOGY

Chairman Dr W R F Luke, 316 Medical Arts Bldg, >  
Toronto, Canada  
Secretary Dr W T Gratton, 216 Medical Arts Bldg,  
Toronto, Canada  
Place Academy of Medicine, 13 Queens Park Time  
First Monday of each month, November to April

WASHINGTON, D C, OPHTHALMOLOGICAL SOCIETY

President Dr S Bockoven, 1752 Massachusetts Ave,  
Washington, D C  
Secretary-Treasurer Dr John Lloyd, 1218-16th St  
N W, Washington, D C  
Place Medical Society of District of Columbia Bldg,  
1718 M St N W, Washington, D C Time 7 30  
p m, first Monday in November, January, March  
and May

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman Each member in turn  
Secretary Dr Samuel T Buckman, 70 S Franklin  
St, Wilkes-Barre, Pa  
Place Office of chairman Time Last Tuesday of  
each month from October to May

# ARCHIVES OF OPHTHALMOLOGY

VOLUME 32 (old series volume 89)

SEPTEMBER 1944

NUMBER 3

COPYRIGHT, 1944, BY THE AMERICAN MEDICAL ASSOCIATION

## PRESENT STATUS OF EYE EXERCISES FOR IMPROVEMENT OF VISUAL FUNCTION

WALTER B LANCASTER, M D

BOSTON

One of the fundamental laws of biology is that repetition of an act facilitates its performance. The first time one does something one may do it clumsily and laboriously, the hundredth time it may be done dextrously and with ease. No principle of physiology and psychology is more firmly established than this. It is, of course, the basis of acquiring skill in any performance. To understand its *modus operandi* one must recall the way the nervous system is organized and how it operates. There are a prodigious number of nerve cells and an intricate network of communicating fibers. These fibers afford pathways for messages—nerve impulses—from one “center,” or group of nerve cells to another and, finally, to a muscle or gland or other effector, unless somewhere along its course the impulse is arrested by inhibitory forces. When an act is clumsily performed, the messages are not passing smoothly and freely along the proper pathways, false turnings must be corrected before the desired end is reached. If the act is repeated over and over again, the passage of the nerve currents in the proper pathways is made easier and more efficient, i e, with fewer false turns or hesitations—is “facilitated” as it is called<sup>1</sup>.

Repetition is the essential feature of exercises, training and learning, as these terms are used here. Obviously, repetition of an act with a faulty method will serve to confirm the fault just as surely as repetition with a correct method will confirm the good habit. This is why the capable coach or trainer or teacher watches early for

faulty performance. For instance, the golfer who practices his swing in a faulty way only confirms his faults, he will improve and, if he has some natural talent, may consistently get below 100, but unless he has a competent teacher, he cannot expect to break 80 except by a rare streak of luck, his play will be erratic and uncertain.

So in orthoptics, for example in bar reading, the more the patient reads in the wrong way, shifting his fixation from eye to eye, so swiftly perhaps that he reads aloud smoothly line after line, the more deeply rooted does his suppression become. The experienced orthoptist could cite many other examples of ways in which exercises, perhaps with automatic electric motor contrivances, cause the patient to make certain movements but do not guard against his carrying them out by a faulty method.

If the act involves muscular performance, as most acts do, the muscles involved increase in size and power (hypertrophy) and become stronger. If the muscles are already strong enough, no increase results from the exercise. For example, in learning to row two things are involved, skill in handling the oars and muscles strong enough to do the work required.

There are many activities which call for increased strength of the muscles, as well as increased skill in using them. This is notably the case if the learning of a given skill is undertaken before the person has reached full muscular development. If a boy of 12 takes up golf, he can learn to swing the clubs with great skill and graceful coordination, but until his muscles become stronger, he cannot strike the ball hard enough to make a long drive. So the man who is strong—has plenty of muscle—will say that the secret of a long drive is the skill and coordination (“timing” he may call it) used, the weak-muscled player will say it is the power one can put into it that makes the ball go a long way. In fact, of course, both skill and power are essential. In faulty ocular movements such as convergence insufficiency, there are still many who think it is strength of muscular power that is lacking.

Read at the Forty-Eighth Annual Session of the American Academy of Ophthalmology and Otolaryngology, Chicago, Oct 13, 1943

1 This statement simplifies too much the matter of learning. The result would be rigidity, lack of flexibility. If repetition, by facilitating the passage of messages along a fixed route, were the whole story, how could one account for the important fact that when one has learned how to do something, one is able to adapt the performance to unexpected variations in conditions which may arise and may call for immediate changes in the way the act is best performed in some of its details?

Others, realizing the great excess of muscular strength that is provided in the ocular muscles, stress the lack of coordination, the inability to use the muscles, the lack of "skill," employing that word in a broad sense

That exercise and practice improve the performance of muscular, or motor, activities no one is likely to deny. In the case of sensory activities there may be certain doubts. How, one might ask, will practice improve sight or hearing? The dioptric images formed on the retina serve as the stimulus, the only way to improve sight is to get a better image on the retina. This cannot be obtained by practice or exercises. This concept of seeing is far from correct. The first step in seeing is the formation of a good image on the retina, by fixation on the best part of the retina, the fovea, but this is only the first step.

It is well established that it is impossible to experience a pure, isolated sensation. There are two factors which affect all sensations as they reach consciousness and become perceptions. The first is concerned with all the other sensations coming into consciousness at the same time through the visual apparatus, and not merely through the visual apparatus but through tactile, kinesthetic, auditory and all other avenues.

The second factor comprises memories of past experiences, and even inherited predispositions. I wish there were time to elaborate on this phase because it is of enormous practical importance in an understanding of how one sees. It explains how a mere glimpse, perhaps in dim light, of an object well known from previous experience, results in one's "seeing" many details which, as a matter of fact, are supplied by memory. For example, the apparent color of a dress may be altered by the color of the lighting under which it is seen, but because one knows from many past experiences what the color is under daylight (white light), the object is "seen" as having its well known, not its apparent, color.<sup>2</sup> So, in even greater degree with apparent size, apparent distance and apparent form, the pattern as a whole is appreciated as a unitary and complete pattern, without any conscious analysis of its individual details. Different stimuli, often apparently contradictory, may produce the same response. A square card seen obliquely makes an image on the retina which is not square, but it is "seen" as square, from whatever angle it is viewed. "The essential factor, therefore, in the emergence of any pattern is its meaning."<sup>3</sup> I must assume that

the reader is thoroughly familiar with these facts, about which volumes have been written.

The memories of past experiences (usually unconscious) affect profoundly the various sensations. It is obvious that exercises and practice serve to build a substratum of experience, a storehouse of memories, which facilitate perception of whatever is the subject of the practice and exercises.

The effects of exercises which I wish to stress are as follows:

- 1 The facilitation of pathways and of conditioned reflexes.

- 2 The accumulation of a fund of experiences, a storehouse of memories and associations, from which are evoked responses by the immediate sensations, which lead to interpretations and which altogether build up and determine the perception. In short, seeing is only half ocular, the other half is cerebral. One cannot say that either half is the more important, since the two are equally indispensable and in practice inseparable.

An effect which I wish not to stress, but to minimize, is the increase in muscular strength which results from exercise.

Examples of the effect on sight of practice or exercises follow:

- 1 Treatment for color blindness in men rejected from military service. The usual procedure called the light and filter treatment, as described by optometrists, consists in the fixation of colored sources of light for several minutes and the use of filters, with a daily check of progress on the pseudoisochromatic plates.

Two instructors in optometry at Ohio State University, Bridgman and Hofstetter,<sup>4</sup> skeptical about this method of improving color vision tested several subjects, 3 of whom had passed the Navy tests successfully after treatments by a practicing optometrist. The authors concluded that their results did not in any way support the assumption that the exercises intended to train color vision are of any assistance. It appeared, on the contrary, that the exercises are merely time consuming and that the improvement in scoring is related only to the learning made possible by repeated testing.

A color-blind subject from the eye clinic tested in the usual way, had a score of 15 of 46 plates in the first test. He was tested four times. He was told when he was wrong but was not given the correct answer. His scores were 27, 35, 43 on the second, third and fourth tests. Similar results were obtained with other subjects. The

<sup>2</sup> Duke-Elder, W. S. *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1933, vol. 1, p. 1019.

<sup>3</sup> Duke-Elder,<sup>2</sup> p. 1023.

<sup>4</sup> Bridgman, C. S., and Hofstetter, H. W. *Improving Color Vision*, *Optom. Weekly* 34:471 (May 27) 1943.

authors showed how this improvement can be explained. They concluded that those who criticize the practice of training color vision are entirely justified. They find no evidence that color filter treatment is effective in improving color blindness. They questioned the type of evidence which has been accepted as a conclusive indication of improvement in color vision. Proof of such improvement can be supplied only by measurement of fundamental color vision functions, such as the Rayleigh Equation. The treatment, they concluded, is not justified since it may lead to the acceptance of responsibilities which the patient cannot fulfil, though he erroneously believes himself cured of color blindness.

This is an excellent piece of work, such as one has learned to expect from the optometry laboratory of Glen Fry. It is to be noted that though the color blindness is not cured, the subjects do learn to see the plates more correctly, an illustration of how practice operates.

2 Peripheral vision.<sup>5</sup> Over 200 subjects were tested under properly controlled conditions. The evidence indicated that peripheral visual acuity can be trained. Twenty per cent of the original group of 100 subjects when retested showed improvement of 16 per cent. The improvement was roughly proportional to the amount of time taken by the test.

3 Speed with which a number of digits or letters are seen. Renshaw<sup>6</sup> reported work on the Polish lightning calculator Dr. Finkelstein, who memorized 8 digits in 0.03 second, 12 digits in 0.824 second and 16 digits in 1.73 seconds. Renshaw then took 12 university students, 2 of whom were able in time to surpass Finkelstein's record. For example, after twelve practice sessions of thirty minutes each, one average student was able to memorize a 12 digit number in 1.5 seconds, although at the beginning it took him 90 seconds. A more highly trained subject memorized a 21 digit number in 4.372 seconds instead of 90 seconds, as in early trials.

Renshaw commented

The difference between the expert and the novice in the rapid and accurate perception of visual material is the same difference as that between the expert and the novice in the performance of any skilful act. We have to learn to see just as we have to learn to swim, to play the piano, or to speak French. This can be done with skill and efficiency, or it can be done haltingly and ineffectively. When we train children to learn to spell English words by replacing the wasteful and ineffective

disjunctive method of seeing words, with the proper method of visual perception, spelling difficulties disappear. Not only does a child spell accurately and easily, but he comes to enjoy spelling. An incidental by-product also is that his rate of reading and index of comprehension automatically show a corresponding improvement.

4 An experiment in which a person with practically normal eyes wears an eikonic lens magnifying one meridian of one eye. This throws his binocular space perception out of gear but does not affect his monocular judgment of space. For a few days, especially in the morning, he is somewhat annoyed by this defect, but as time goes on he learns to suppress his faulty binocular perceptions and rely on his monocular clues. If he is placed in an environment in which monocular clues are few or absent, he is much disturbed. Since most situations present abundant monocular clues, a room for instance, he is aware of little or no effect on his seeing. He has learned to adapt himself to the new conditions.

5 Orthoptic training for heterophoria or heterotopia.

(a) A bookkeeper did his work laboriously and more slowly than he ought, with too many errors and with undue fatigue and frequent headaches. He had considerable heterophoria, with suppression which made it unduly difficult to follow lines across the paper correctly and to add up columns of figures. A few weeks' training by an orthoptist, with faithful home work, resulted in his learning how to use his eyes more skilfully, so that his work was made easy and rapid, with greatly reduced fatigue.

(b) A girl aged 12 years had accommodative convergent strabismus with hypermetropia of 3 D and slight astigmatism. Convergence without glasses was 25 prism diopters, and with glasses, 5 prism diopters (with the eyes cosmetically straight). Her mother did not want her to wear glasses. A few months' training by an orthoptist resulted in the patient's learning to hold the eyes straight without glasses.

(c) A child with convergent strabismus and amblyopia of the left eye first learned to see with the amblyopic eye by occluding the right eye, he next learned simultaneous perception, then fusion, then stereoscopic depth perception on the synoptophore and, finally, good binocular vision as a habit, i.e., not merely on the synoptophore but in casual seeing.

6 True myopia. An important group of patients with true myopia and other defects earnestly desire to get rid of their glasses. They have been told by an ophthalmologist or optometrist that they must wear glasses all the time. They go to a follower of Bates who tells them to dis-

<sup>5</sup> Low, F. N. Studies on Peripheral Visual Acuity, Science 97: 586 (June 25) 1943.

<sup>6</sup> Renshaw, S. Psychology of Vision, released through the optometric extension program, Duncan, Okla., 1939 to 1942.

card their glasses, which are crutches. To their surprise, nothing serious happens! Their sight, of course, is still blurred for distant objects, but they find that by practice they acquire the ability to make out objects better through the blur than they did when they wore glasses constantly. They are apt to exaggerate this gain in talking about it.

A young man who had been wearing concave lenses asked if there was any way he could pass the test for 20/20 vision. Vision was 20/15 with glasses but was 20/30 without glasses. He was given a +1.00 D sphere for each eye to wear constantly for three days. His visual acuity was 20/15 without glasses and 20/15 with a +0.50 D sphere, and he read some letters of the 20/20 line with a +1.00 D sphere. Was his myopia cured? No, because he did not have myopia to begin with. He learned to relax his accommodation. He was judged to be myopic by some one because when a -0.50 D sphere was placed before his eye, he said, "that is better, clearer." That a young man with 20/15 vision sees better with a -0.50 D sphere shows that he has good accommodation, not that he has myopia. Other evidence is necessary before such a diagnosis is justified. He should read one or two lines more with the minus glass than he reads without it.

In each of the examples I have cited, the progress of the patient depended on his learning to use his eyes better. He learned to see the isochromatic plates better only by greater skill or proficiency in interpreting his visual sensations. In the first case, the sensations were no better, he was still color blind, but he had learned to make so much better use of his defective apparatus that he fooled the examiner. Another learned to see better with the peripheral portion of his retina not because the sensations were better or the retinal images better, but because he had learned by practice to perform better the cerebral processes which are an important part of seeing. The third subject learned to take in a group of figures in a small fraction of the time it required at first not because his visual sensations had improved, but because he had learned how to use them by practice, by exercises. The man who experimented with eikonic lenses became adapted to them by practice, by learning to suppress what was not to his advantage to "see" and to utilize instead what he found to be dependable, and therefore advantageous. Perhaps one might think the bookkeeper with the heterophoria derived his relief from strengthening certain weak muscles. This I stoutly deny. His muscles

were not weak when he began, and they were not notably stronger when he had recovered from his disability. His bad habits had been changed to good ones by skilfully directed exercises and practice. Probably he had been suppressing, for one thing, and that certainly cannot be cured by strengthening muscles. The patient with accommodative convergent strabismus learned to use her muscles so as to hold the eyes straight by relaxing certain muscles, not by strengthening them. The seventh case is the most beautiful demonstration of all. The amblyopia was cured by exercises, by practice, by learning to see. The patient was guided skilfully through the intricacies of acquiring binocular vision, in its various stages, to a complete cure. Does any one think the secret was in strengthening certain muscles—in this case the lateral rectus muscle?

The eighth illustration shows how much can be gained in learning to see by persistent practice, even when the visual acuity is low. Here belong the patients who acquire improved speed and accuracy of recognition through practice when the question is not one of improvement in visual acuity—the sailor, the airman, the hunter, the fisherman, the prospector, all acquire by practice, i.e., by exercise, the ability to see better, though the visual acuity remains the same. The last example shows how the wearing of a concave lens can induce such a tonic contraction of the ciliary muscle as to counterfeit myopia and how the wearing of a convex lens may induce relaxation by a few days of practice in learning how to see.

I have tried to make it clear that exercises and practice are effective in learning to see better or to use the eyes better in many ways. Use is made of these principles in other branches of medicine, notably, in orthopedics, in which posture is corrected and various disabilities are relieved. Lately, the Kenny treatment for infantile paralysis has been in the limelight. It has achieved some brilliant results. The explanations given by the originator of the method have been shown by competent investigators<sup>7</sup> to be false, but that is not sufficient reason for abandonment of the treatment, the good points of which should be adopted.

Similar comments may be made about the Bates treatment, lately given such publicity by Huxley, by other authors and by numerous

7 Moldaver, J. Physiopathologic Aspect of Disorders of Muscles in Infantile Paralysis, *J. A. M. A.* **123** 74 (Sept 11) 1943. Watkins, A. L., Brazier, M. A. B., and Schwab, R. S. Concepts of Muscle Dysfunction in Poliomyelitis Based on Electromyographic Studies, *ibid.* **123** 188 (Sept 25) 1943.

articles in the lay press<sup>8</sup> The number and prominence of these articles are evidence that the public is interested Several editorials and reviews have appeared in professional journals<sup>9</sup> Notice was taken of the problem by the National Committee on Optics and Visual Physiology at its last meeting in June 1943 It is not surprising, therefore, that the secretary selected this subject as suitable for discussion here

If one studies the various publications with an open mind, searching for the things which will explain why the public wants this treatment, one will be forced to admit that buried in a mass of what to ophthalmologists seem foolish gestures and performances, best defined as hocus-pocus,<sup>10</sup> there are sound and fruitful ideas It is these that account for the survival and spread of the cult It certainly is not foolish to believe that people can be taught to use their vocal organs in speaking or in singing, that they can be taught to play musical instruments, to dance, to skate and to play games, such as billiards or golf, and, as a result of teaching, can learn to perform better than they can without instruction and training In the same way, the public argues, they should be instructed in the use of their eyes They consult the ophthalmologist and are provided with glasses, but are given little information about the nature of their trouble or about measures which might help them to use their eyes successfully Yet they hear of some one who went to a follower of Bates and got plenty of instruction There are many, very many, patients who do not want to wear glasses, who would go to almost any length to escape that fate This should be taken account of in dealing with such patients The alternatives should be

pointed out Most of them appreciate having things explained to them This takes time and patience, but the physician need not do the teaching himself, he can employ some one to do it for him Thus he can be sure it is done right The patient is given sound instruction, not mixed with hocus-pocus The patient, of course, cannot discriminate between the pseudoscience of the partly educated followers of Bates and the sound truths of the well trained ophthalmologist

However, it is important to point out that the hypothetic well trained ophthalmologist is often ignorant of certain phases of the art and science of which he is supposed to be master He is apt to make the mistake of arguing that because Bates's theory of accommodation is incorrect, his whole program is unsound The history of medicine is a long list of tentative theories later proved to be erroneous, but the facts they tried to explain remain firmly established, though the theories are swept away Quinine cured malaria and continued to cure it, though the theories invented to account for its action were entirely erroneous Likewise, lime juice cured scurvy and so on

Among the important things emphasized by Huxley are The value of relaxation and the harm of tension, the pernicious influence of fear, e g, fear of light, fear of blindness, fear of using the eyes, the dual nature of seeing—sensation plus interpretation equals perception—and the necessity of giving attention and treatment to the cerebral side of the function<sup>11</sup> The fact that in carrying out treatment along these lines the method indulges in numbo-jumbo should not prevent one from making use of the good points concealed therein

Then, with a sounder theoretic basis, and therefore more intelligent execution, the good results will be still more impressive Orthoptics manages to cure certain of the conditions for which it is used by a more or less clumsy routine based on the erroneous theory that some muscle needs to be strengthened With a more skilful technic, based on a wiser, more rational, theory, the progress is far more rapid and sure in the hands of persons who know how to apply the better methods

#### SUMMARY

There is abundant evidence for the general proposition that exercises, repetition, practice

11 It is often pointed out that Huxley's visual acuity has not improved in any extraordinary way He admits that The point is that he has learned how to use what he has to better advantage It is not the primary retinal sensation that is improved, it is the neglected, but vitally important, cerebral part of seeing that has been trained

8 (a) Huxley, A L The Art of Seeing, New York, Harper & Bros, 1942 (b) Bates, W H Perfect Sight Without Glasses, New York, Central Fixation Publishing Co, 1920 (c) Corbitt How to Improve Your Eyes, Los Angeles, 1930 Ross, J A, and Rehner, L How to Get and Keep Good Eyesight, Garden City, N Y, Sun Dial Press, Inc, 1943 Huxley, A L Learning to See, Collier's 111 24 (April 12) 1943 Barendsfield Aldous Huxley's Seven Years in America, Book Review, New York Times, June 27, 1943

9 (a) Sorsby, A, cited by Huxley,<sup>8a</sup> Appendix I (b) Duke-Elder, W S The Art of Seeing, by A L Huxley, Book Review, Brit M J 1 635 (May 22) 1943, Arch Ophth 30 582 (Oct) 1943 (c) Crisp, W H More About Eye Exercises, Am J Ophth 26 872 (Aug) 1943 (d) Pascal, J I On Aldous Huxley's "The Art of Seeing," ibid 26 636 (June) 1943 (e) Aldous Huxley's Vision, editorial, J A M A 122 951 (July 31) 1943

10 Duke-Elder<sup>9b</sup> referred to them as "Huxley's antics of palming, shifting, flashing, and the rest are probably as good treatment as any other system of Yogi or Coue-ism"

and learning lead to better performance, to the acquisition of skill<sup>12</sup> Many ocular conditions exemplify this law Since seeing is only partly a matter of the image on the retina and the sensation it produces, but is in still larger part a matter of the cerebral processes of synthesis, in which memories play a principal role, it follows that by repetition, by practice, by exercises one builds up a substratum of memories useful for the interpretation of sensations and facilitates the syntheses which are the major part of seeing Also, motor functions are perfected by practice, by learning, and reflex pathways are facilitated

12 Here are some quotations from Huxley<sup>8a</sup> "The art of seeing does not stand or fall with any particular hypothesis [page 33]"

"The art of seeing is like other fundamental or primary psycho-physical skills, such as talking, walking and using the hands"

"People may have the most fantastic views about physiology, but this will make no difference so long as their theory and practice of psycho-physical functioning remain adequate to their purpose If psycho-physical skills depended for their development on a correct knowledge of physiology, then nobody would ever have learnt any art whatsoever It is probable, for example, that Bach never thought about the physiology of muscular activity, if he did it is quite certain that he thought incorrectly That, however, did not prevent him from using his muscles to play the organ with incomparable dexterity [page 34]"

Ophthalmologists have neglected this field and have concentrated their attention on the primary source of the sensation, the image on the retina, leaving to irregular, half-trained workers the cultivation of that field The achievements obtained by the clumsy practices which have been developed should stimulate ophthalmologists to investigate and discover the valuable possibilities in this field which, I am convinced, await intelligent development Finally, in assessing the value of exercises it must not be forgotten that many patients have a neurotic or psychic element and that such patients are often favorably affected by hocus-pocus Do not make the mistake of thinking that this is the whole story

I have said nothing about actual structural changes which are wrought by exercises, other than hyperplasia and hypertrophy of muscles and the consequent changes induced in tendons, and perhaps in bones Frankly, I am skeptical of such an effect A clearing of corneal opacities often occurs to a rather slight degree, but not by means of exercises I doubt whether any changes in size or shape of the eyeball are brought about by such means Certainly, the burden of proof is on those who make such claims Permit me to quote Jesus, who said "Which of you by taking thought can add one cubit unto his stature?"



# PARTIAL RESECTION OF THE LID AND PLASTIC REPAIR FOR EPITHELIOMA AND OTHER LESIONS INVOLVING THE MARGIN OF THE LID

ALGERNON B REESE, M D

NEW YORK

It is frequently advisable to excise an epithelioma involving the margin of the lid, and technics which I have found satisfactory for doing this will be described here

The principle, which is based on the use of a sliding graft from the temple, is not new, and even the particular methods given here have been employed in general by others. For the most part, these technics were used by Wheeler<sup>1</sup>. I describe them here for the purpose of mentioning certain modifications and emphasizing certain steps which I have deemed important in the performance of 34 such operations

It is not within the scope of this article to discuss the relative merits of irradiation and surgical procedures in the treatment of epithelioma of the lid. Suffice it to say that in my opinion surgical treatment seems to be the therapy of choice in most instances. Operation is usually adequate to control the growth, gives a better cosmetic result and leaves a more comfortable and better functioning eye and lids. It enables the patient to forego the frequently untoward sequelae of irradiation, such as defect in the cilia line and the margin of the lid, atrophy and telangiectasis of the adjacent skin, new-formed and dilated blood vessels of the conjunctiva, keratinization of the palpebral, bulbar and even the corneal epithelium, and cataract. In cases of recurrence of the epithelioma after irradiation, further irradiation is sometimes contraindicated, and surgical intervention is imperative. In other cases, when the lesion is extensive, irradiation should be carried out first and the operation here described done later in order to repair the residual defect in the lid (fig 16 *A*, *B*, *C*, and *D*). These operations can also be used to excise a nevus and a hemangioma of the margin of the lid and to repair a congenital (fig 17 *A* and *B*) or a traumatic (fig 18 *A* and *B*) coloboma of the lid

Read before the New England Ophthalmological Society, Jan 18, 1944

From the Institute of Ophthalmology of the Presbyterian Hospital and the Memorial Hospital for the Treatment of Cancer and Allied Diseases

<sup>1</sup> Wheeler, J M. Collected Papers of John M. Wheeler. New York, Columbia University Press, 1939, pp 338-342

A good cosmetic result may be expected. There should be no defect in the continuity of the lid margin or the cilia line at the site of the anastomosis, and there should be a good cul-de-sac. It is fortunate that most epitheliomas of the lid involve the lower lid, for the lower lid is more easily repaired than the upper. The operations can, however, be employed satisfactorily on both lids. The technics as applied to the lower lid will be described, and any modifications necessary for their employment on the upper lid will be mentioned

When the lesion to be excised requires the resection of approximately one third or less of the length of the lid, a somewhat simpler procedure can be carried out than when a greater resection is necessary. The decision as to whether the operation for the lesser or the greater resection should be employed depends a great deal on the individual case. When the lid is lax, as it is likely to be in some persons, especially in older patients, the simpler procedure can be used to fill a larger defect than would otherwise be possible

The simpler procedure is as follows. Local infiltrative and block anesthesia are satisfactory. With a Graefe knife the lid is halved on each side of the lesion for 3 to 4 mm (fig 1). The distance from the lesion at which the halving is started depends on the distance the lesion infiltrates. The halving should be started beyond the limit to which the lesion is thought to extend<sup>2</sup>

The external half of the lid should include skin, cilia and orbicularis muscle, while the internal half should include conjunctiva and tarsus. The depth to which the halving extends depends on the width of the piece of lid to be resected, but usually the distance is 6 to 8 mm

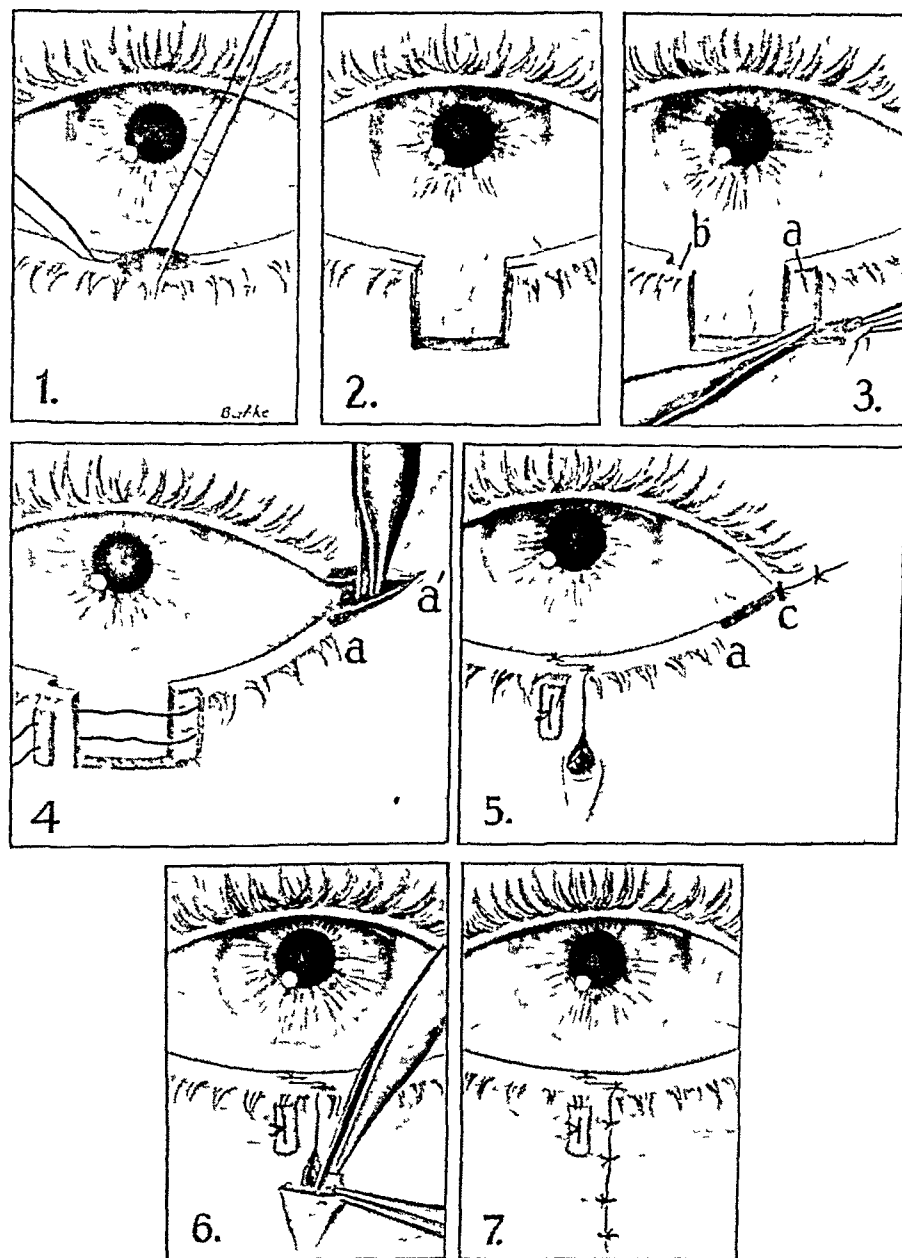
A silk traction suture is passed through the lesion to facilitate manipulation (fig 1). The lesion is excised by removing the desired amount of lid in the shape of a square or rectangle (fig 2). This consists of a block resection of the entire thickness of the lid, including the conjunctiva. A square or rectangle is better than

<sup>2</sup> The drawings for both of the operative procedures show the excision close to the lesion, a nevus. The distance from the lesion the excision should be made depends of course on the individual case



a V because less lid margin has to be sacrificed and the anastomosis can be made more accurate. The anterior half of the lid at one edge is then excised over the region which was halved (fig 3 *a*), and the posterior half of the other edge is excised over the region which was halved (fig 3, *b*). An external canthotomy is then done, its direction being slightly upward to follow the contour of the lower lid (fig 4,

suture should be so placed that there is overcorrection when the halved edges come together. The release of the lateral portion of the lid at the external canthus should be sufficient for the halved edges to approximate easily without requiring tension on the double arm suture. The double arm suture is then tied over a rubber pig (fig 5). This leaves a puckering of the skin below the lid anastomosis (fig 5). A



Figs 1-7—Excision of nevus by the procedure of halving

*a* to *a'*) Scissors are inserted in the canthotomy opening between the skin and the conjunctiva, and the lower portions of the external canthal ligament are incised until the external portion of the lower lid is sufficiently released to permit it easily to fill the defect left by the resection. A double arm silk suture is then placed through the posterior lip of the halving and carried through the anterior lip (fig 4). This double arm silk

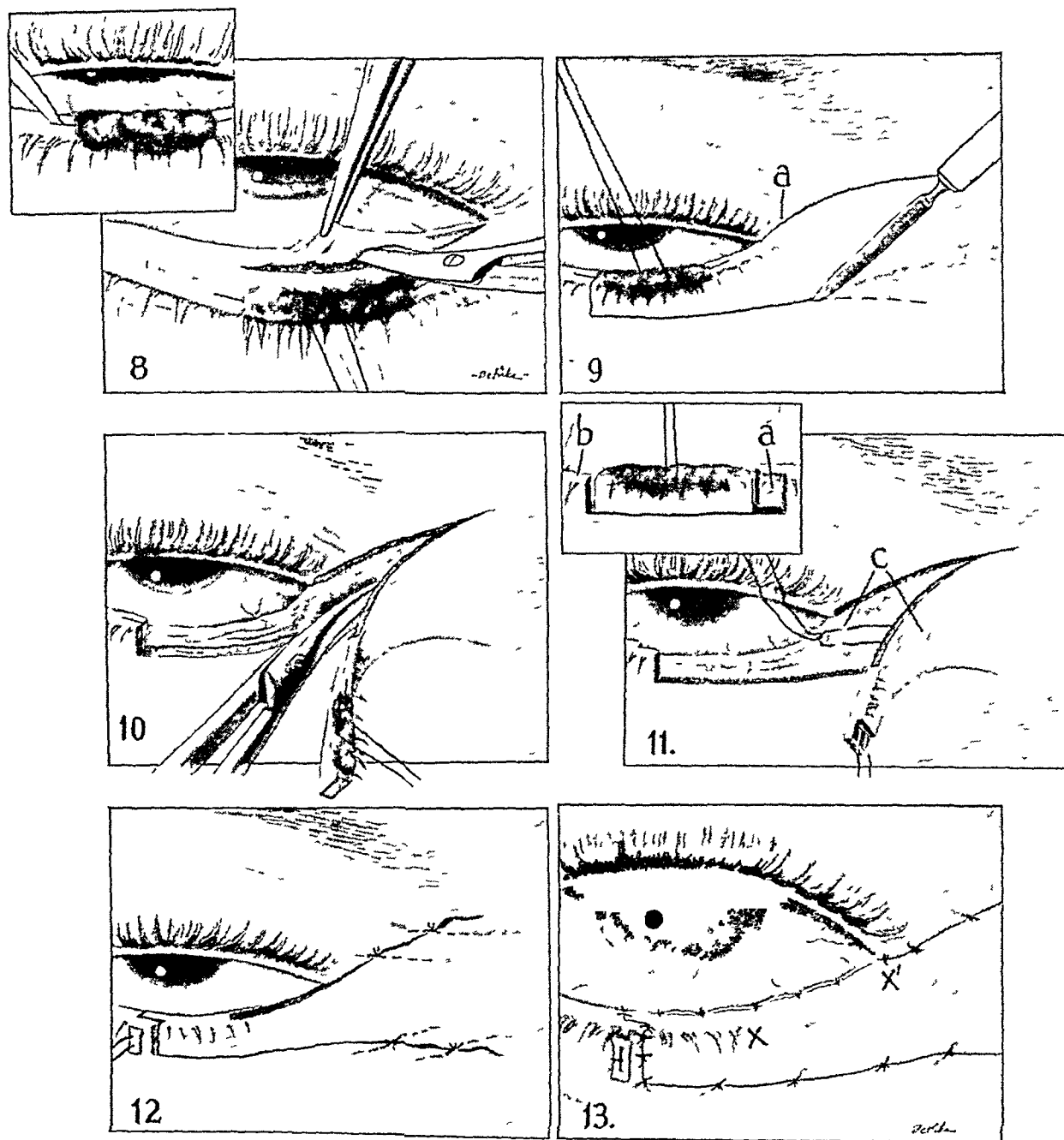
triangular piece of this skin is excised (fig 6), and the edges of the skin are approximated with silk sutures (fig 7). Several sutures can be used to approximate the halving along the margin of the lid if necessary. An interrupted silk suture is placed at the point designated as *C* in figure 5 to determine the new external canthus, and several other interrupted silk sutures are placed to approximate the edges of

the skin over the site of the external canthotomy. This leaves an area from *a* to *c* (fig 5) to form the new-formed lid margin, and along this edge no further suturing is necessary. The same technic is applicable to both the upper and the lower lid.

A result using this technic is shown in figure 14 *A* and *B*.

When the lesion to be excised requires the resection of more than one-third the length of the lid, a more extensive operative procedure is

(fig 8). As much as possible of the conjunctiva of the lid is salvaged. With the exception of that portion firmly adherent to the tarsus, all the conjunctiva can usually be saved unless the lesion extends through the entire thickness of the lid to involve the conjunctiva. This dissected and free conjunctiva is now pushed down into the cul-de-sac and forgotten till the end of the operation. With a scalpel, the amount of the lid to be included in the resection and sliding graft is outlined on the skin (fig 9). This should



Figs 8-13—Resection of a portion of the lid, with repair by a sliding temporal graft

indicated, a description of which follows. Local infiltrative and block anesthesia are satisfactory. The halving is carried out in the same manner as described in the previous procedure (fig 8, insert).

A silk traction suture is passed through the lesion to facilitate manipulation of the lid (fig 8). The conjunctiva is dissected from the posterior surface of the lid to the cul-de-sac

be so fashioned that the incisions diverge temporally to make the base of the graft progressively broader for nutritional purposes. Rather than to continue the upper temporal cutaneous incision in line with the lower lid, it is better to carry it somewhat higher (fig 9, *a*). In any case, caution should be taken not to carry it lower. This suggestion is advisable because of a tendency to a slight depression of the lid

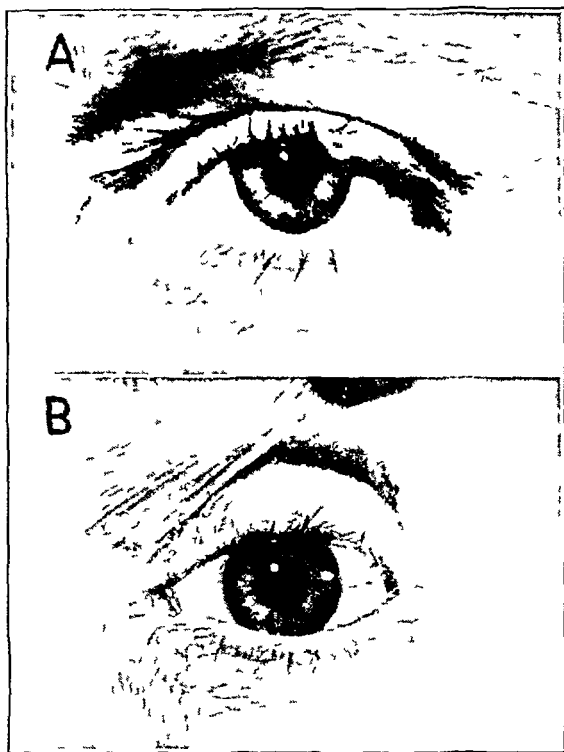


Fig 14—*A*, basal cell epithelioma of the right upper lid, proved microscopically. It was necessary to resect approximately one third of the lid. The procedure shown in figures 1 to 7 was carried out. There was sufficient uninvolved lid margin at the temporal side for the anastomosis. The patient was well two years after operation.

*B*, right eye of the patient one year after operation.

margin at the junction of the old and the new lid margin.

The vertical incision through the lid nasally is now completed, as well as the horizontal incisions, and the portion to be resected, as well as the portion to be included in the sliding graft, is dissected free into the temporal region (fig 10). The distance into the temporal region to which the dissection is carried depends on the amount of the defect to be filled by the sliding graft. Up to this point, if the lesion is not ulcerated and infected, that portion of the lid which is to be resected has not been removed. It is left intact in the interest of easier manipulation of the lid during the dissection. The part of the lid to be resected is now excised (fig 11, insert). The remaining margins of the lid are now prepared for the halving procedure, as described in the previous operation. The anterior half (cilia, skin and orbicularis muscle) of the temporal edge is excised over the region which was halved (fig 11, inset *a*), and the posterior half (tarsus and conjunctiva) of the nasal edge is excised over the region which was halved (fig 11, inset *b*). The skin and cilia should be left on the nasal side, so that they can benefit by the established blood supply of this

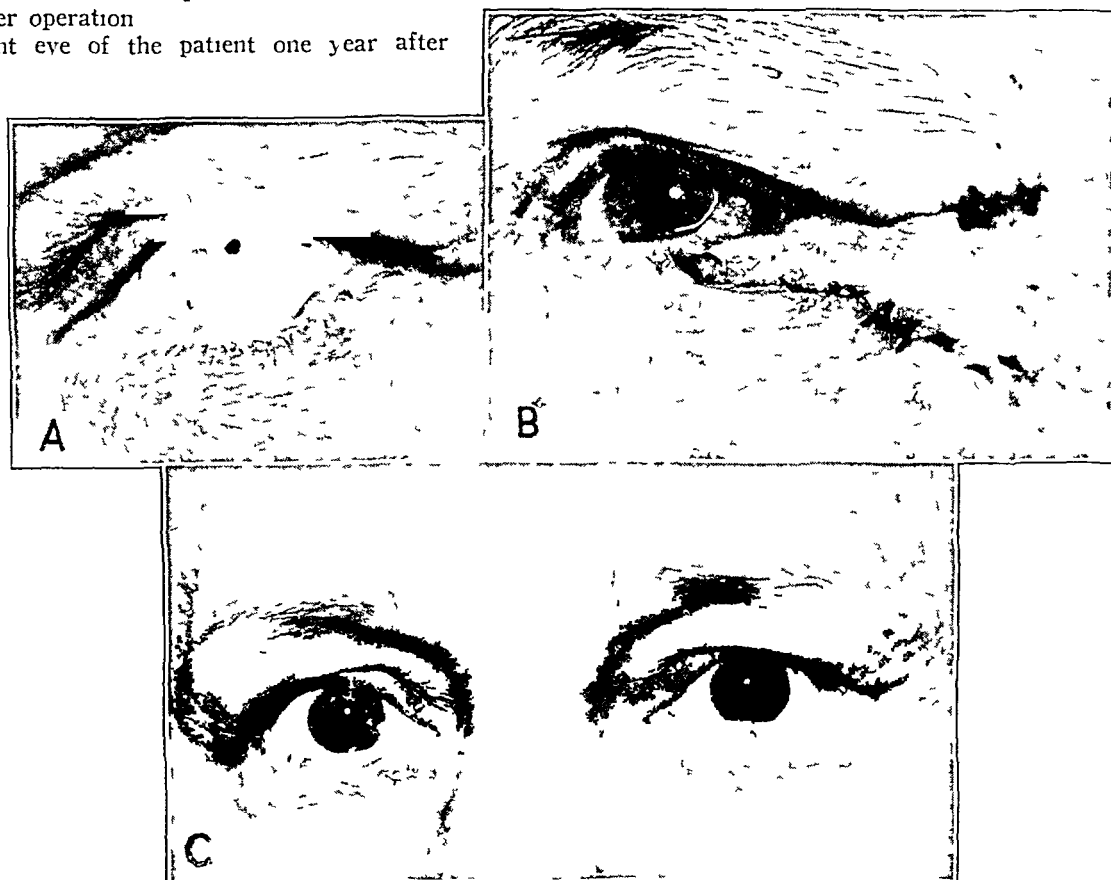


Fig 15—*A*, a basal cell epithelioma of the right lower lid, proved microscopically. The lesion had infiltrated to a considerable extent, so that it was necessary to resect approximately one half of the lid. The procedure shown in figures 8 to 13 was carried out. There was sufficient uninvolved lid margin temporally for the anastomosis. The patient was well four years after operation.

*B*, site of operation on the fifth postoperative day, with sutures in place.

*C*, appearance one year after operation.

portion of the lid. That portion of the sliding graft which will participate in the new part of the lower lid should be thin, but the graft should then become progressively thicker toward its base. A double arm silk suture is placed through the complementary halves of the lid margin so that there will be some overcorrection of the anastomosis, as described in the previous opera-

unite the margins of the skin. It is important to place accurately an interrupted silk suture to determine properly the new external canthus (fig 13,  $x'$ ). The edge of the palpebral conjunctiva is now united to the lid margin with interrupted plain surgical gut sutures (fig 13). The new lid margin is now between  $X$  and  $X'$  (fig 13). In order to accomplish the necessary pull of the graft toward the defect to be filled, the placing of interrupted silk sutures may occasion some puckering of the skin. This can be ignored, as it smooths out and causes no untoward blemish.

When the defect to be filled in the lid is large, it is not sufficient to make the upper horizontal incision only, for this will produce a tendency in the lid margin to evert. This tendency is overcome by making the lower horizontal incision.

A result using this technic is shown in figure 15, *A*, *B* and *C*.

The same procedure can be applied to the upper lid. On the upper lid, however, it is

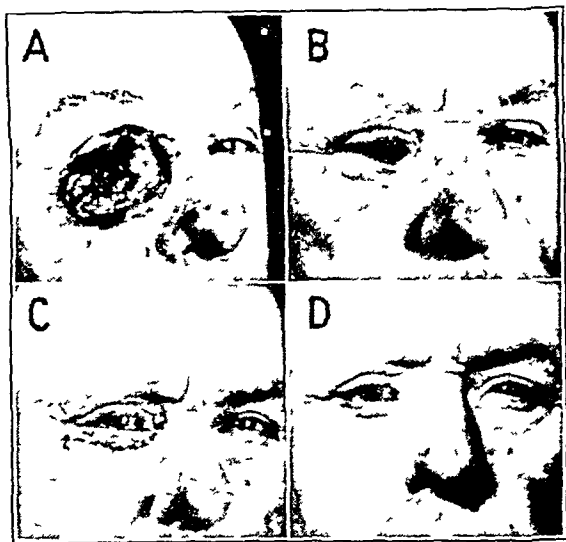


Fig 16—*A*, an extensive ulcerated and fungating basal cell epithelioma, involving mostly the lower lid.

*B*, disappearance of the lesion after roentgen irradiation, leaving a defect in the lower lid.

*C*, result of plastic repair of the defect by the procedure described in figures 8 to 13, as seen on the ninth postoperative day, with sutures in place.

*D*, patient one and one-half years after operation. He is still well, five years after operation.

tion. The temporal flap should have been sufficiently undermined to permit a comfortable sliding of the graft to fill the defect. A subcutaneous double arm surgical gut suture should be placed under the temporal flap and passed through the periosteum at the external orbital margin (fig 11 *c*) in such a manner that when the suture is tied the temporal flap will be slid nasally to fill the defect. The temporal flap is pulled farther nasally by interrupted silk sutures so placed that when tied they draw the flap toward the defect (fig 12). This should be accomplished mainly by sutures placed along the lower horizontal incision rather than the upper, because the upper edge of the skin is more lax and if too much pull is attempted here the upper lid will be pulled laterally, with a tendency to lengthen and narrow the palpebral aperture. The double arm silk suture uniting the halved portions of the lid is now tied over a rubber pig (fig 13). In order to minimize the chances of interference with the nutrition of the tip of the graft, with production of slough, no tension should be put on this suture in uniting these complementary portions of the lid margin, and the suture should not be tied too tight. Interrupted silk sutures

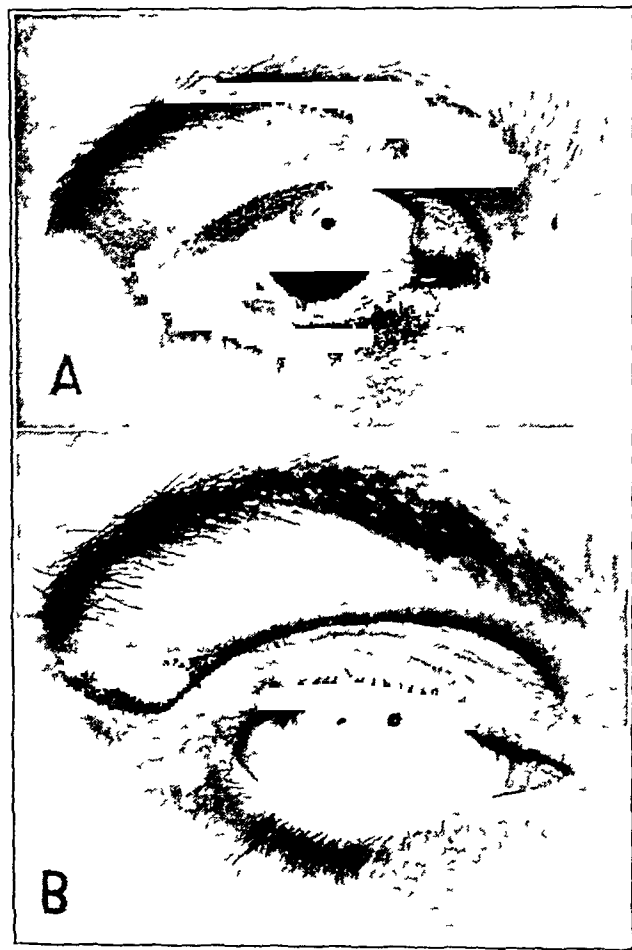


Fig 17—*A*, congenital coloboma of the right upper lid. *B*, repair of the lesion by the procedure described in figures 8 to 13.

somewhat more difficult to secure the necessary pull for sliding the temporal graft over to fill the defect in the lid. This is true because the lower edge of the skin is continuous with the mobile lower lid and the upper edge of the skin is lax. On the upper lid it is necessary, therefore, to carry out the dissection farther temporally and

to rely less on pull from suturing. When the operation is done on the upper lid, there is no material interference with the levator function, provided several plain surgical gut sutures approximate the severed levator muscle to the upper margin of the remaining tarsus and the conjunctiva and edges of the skin are well approximated. Dissection of the conjunctiva from the upper lid must start at the upper margin of the tarsus because over the tarsus the con-

can be used to repair any amount of defect in the lower lid (even one involving the entire lower lid), it is not applicable to repair more than one half of the upper lid.

In any halving procedure on the lid, a more satisfactory anastomosis is obtained between actual lid margins than between a lid margin and skin. However, it is necessary to anastomose lid margin to skin when the lesion to be excised is so close to the external or the internal canthus

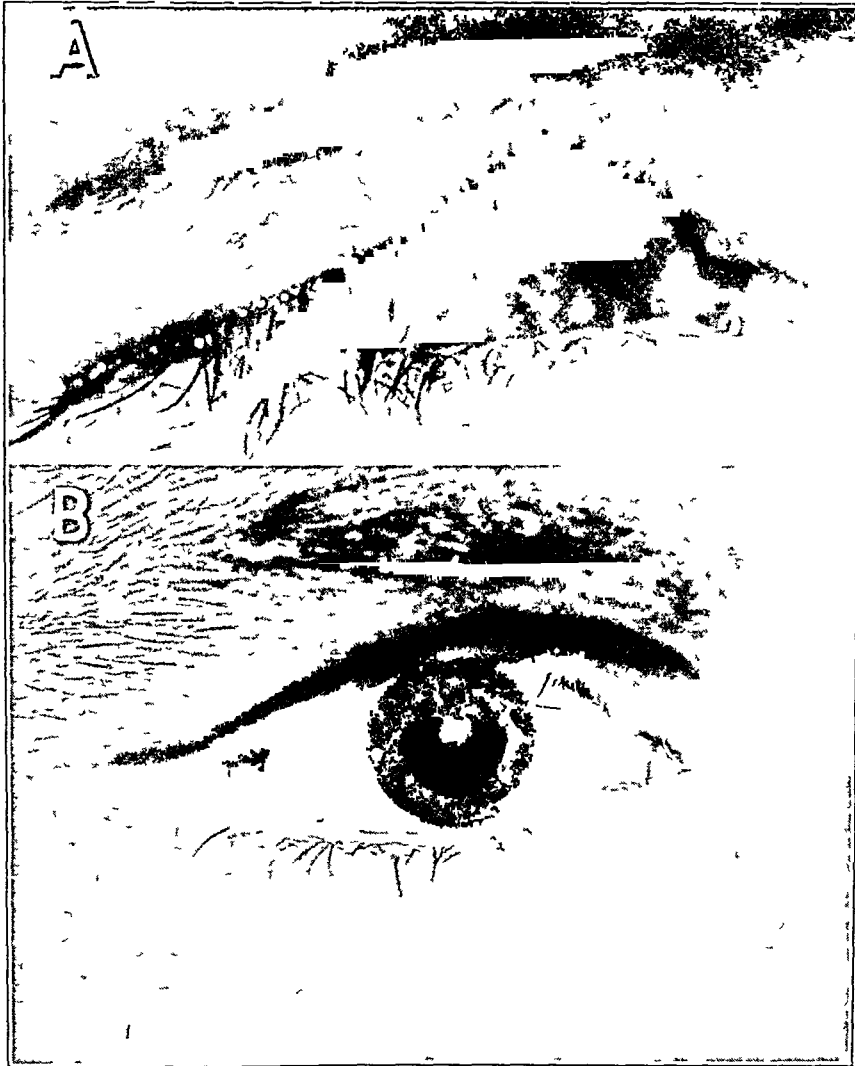


Fig 18—*A*, traumatic coloboma of the upper lid sustained in an automobile accident from laceration with glass. The globe was enucleated, and the patient could not wear a prosthesis because of cicatricial contraction of scar tissue in the coloboma. The cul-de-sac was obliterated by the scar over its course posteriorly. A block resection of the coloboma and adjacent scar was done by the procedure described in figures 8 to 13.

*B*, prosthesis worn six months after operation.

conjunctiva is too adherent. Since this region is inaccessible at the completion of the operation unless undue strain is put on the lid anastomosis, it is necessary to do the conjunctival suturing before this anastomosis is completed. Regardless of how much the lid is to be resected, the width of the resected portion should always be sufficient for the upper horizontal incision to extend along the normal horizontal fold of the upper lid. While the procedure described here

that no lid margin is available on one side. Also, when one side of the anastomosis is beyond the termination of the tarsus, and therefore does not include tarsal tissue, the approximation of the two edges of the lid is not accurate, because the double arm suture yields more on the side without tarsal tissue. In such instances, the sliding graft should be more extensively undermined to permit a more generous slide.

73 East Seventy-First Street

# EXPERIMENTAL STUDY ON PENICILLIN TREATMENT OF ECTOGENOUS INFECTION OF VITREOUS

LUDWIG VON SALLMANN, M D , KARL MEYER, M D , PH D ,  
AND JEANETTE DI GRANDI, B A

NEW YORK

In general, ectogenous infections of the vitreous respond unsatisfactorily to any type of therapy. The stimulation of the humoral and cellular body defenses by fever treatment and shock therapy and by local methods, such as withdrawal of small amounts of vitreous (Elschnig,<sup>1</sup> Lowenstein and Samuels<sup>2</sup> and Zur Nedden<sup>3</sup>) did not as a rule prevent the loss of function in the diseased globes. The topical and systemic chemotherapeutic procedures of former days barely improved the unfavorable prognosis. The present potent and less toxic antibacterial agents, such as the sulfonamide compounds and penicillin, introduced iontophoretically and supplemented by systemic treatment, did not check experimental endophthalmitis when the infection had spread from the anterior segment to the vitreous space.<sup>4</sup> These results were not surprising in view of the slow metabolism of the vitreous and its anatomic position in relation to the main portals of entry of drugs into the eye, that is, to the capillaries of the ciliary body and to the cornea. For example, the concentrations of sulfonamide compounds in the vitreous after systemic use ranged, according to Bellows and Chinn,<sup>5</sup> from 0.9 to 5.8 mg per hundred cubic centimeters, only traces of sulfadiazine were found in the vitreous after corneal iontophoresis, despite the high concentrations secured in the

anterior part of the eye.<sup>6</sup> Attempts failed to increase the concentration of sulfadiazine in the vitreous by transscleral iontophoresis.<sup>7</sup> Penicillin, also, did not enter the vitreous in detectable amounts with either local or systemic administration.<sup>8</sup> Because of the failure of the aforementioned methods to produce adequate concentrations of the chemotherapeutic agents in the vitreous, direct injection of the drug into the vitreous space, hazardous as it seemed, was considered as a possible solution. The low tissue toxicity and the high bacteriostatic action of the newer chemotherapeutic agents reduced some of the objections to the procedure.

The study dealt, first, with the distribution of the drugs in the intraocular fluids at various intervals after their intravitreal injection, second, with the damage to the inner structures of the eye attributable to the mechanical trauma and to the toxic action of the injected compounds, and, third, with the therapeutic effect of the selected drugs on a well standardized destructive infection of the vitreous.

## I DISTRIBUTION OF PENICILLIN AND SULFACETIMIDE IN INTRAOCULAR FLUIDS FOLLOWING INTRAVITREAL INJECTION

Penicillin was selected as the most promising representative of the mold products, sulfacetimide was chosen from the group of sulfonamide compounds because of its almost neutral  $p_H$  in solutions of high concentration and because of its effectiveness in various experimental infections of the cornea.<sup>9</sup>

This study was supported by the Knapp Memorial Foundation

Read in part before the New York Society for Clinical Ophthalmology, May 1, 1944

From the Department of Ophthalmology, Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology, Presbyterian Hospital

1 Elschmig, A. Ueber Glaskorperersatz, *Arch f Ophth* **80** 514, 1911

2 Lowenstein, A., and Samuels, B. Ueber Glaskorperersatz, *Arch f Ophth* **80** 500, 1911

3 Zur Nedden, M. Ueber Glaskorperabsaugungen, *Verhandl d ausserord Tag d ophth Gesellsch* (1921), 1922, p 153

4 von Sallmann, L. Penicillin and Sulfadiazine in the Treatment of Experimental Intraocular Infection with *Pneumococcus*, *Arch Ophth* **30** 426 (Oct) 1943

5 Bellows, J., and Chinn, H. Penetration of Sulfadiazole in the Eye, *Arch Ophth* **25** 294 (Feb) 1941

6 von Sallmann, L. Sulfadiazine Iontophoresis in *Pyocyanus* Infection of Rabbit Cornea, *Am J Ophth* **25** 1292, 1942

7 Unpublished experiments

8 von Sallmann, L., and Meyer, K. Penetration of Penicillin into the Eye, *Arch Ophth* **31** 1 (Jan) 1944

9 (a) Robson, J. M., and Scott, G. L. Local Chemotherapy in Experimental Lesions of the Eye Produced by *Staph Aureus*, *Lancet* **1** 100, 1943, (b) The Production and Treatment of Experimental *Pneumococcal* Hypopyon Ulcers in the Rabbit, *Brit J Exper. Path* **24** 50, 1943 (c) von Sallmann<sup>6</sup>

**Technic**—Experiments were carried out on chinchilla rabbits under general anesthesia induced with pentobarbital sodium and local anesthesia induced with 0.1 per cent nupercaine hydrochloride. Two-tenths cubic centimeter of a solution containing 25 milligrams of sodium penicillin per cubic centimeter (10 per cent), or a like amount of a 10 per cent solution of sodium sulfacetamide, was injected into the vitreous under sterile conditions after withdrawal of the aqueous. The injection was made with a fine (27 gage) needle, which was thrust into the vitreous in the region of the equator on either side of

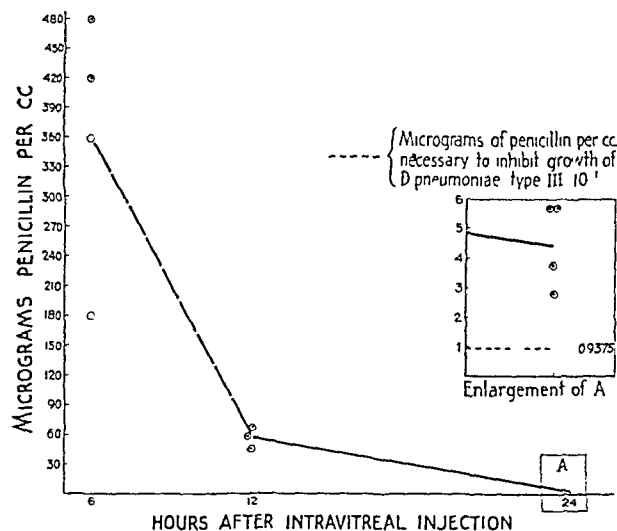


Fig 1—Concentration of penicillin in the vitreous of rabbits after a single intravitreal injection of 0.2 cc of a solution containing 25 milligrams of sodium penicillin per cubic centimeter

the superior rectus muscle. Damage to the lens and to the retina, other than puncture of the latter, was generally avoided by the use of a short, sharp needle. To reduce the trauma of the insertion of the needle into the eye softened by the removal of aqueous, the technic was modified by introducing the needle into the vitreous first, then withdrawing the aqueous and finally injecting the solution of the chemotherapeutic compound. Samples of aqueous and vitreous fluids were taken six, twelve and twenty-four hours after the injection of penicillin for its quantitative determination (four determinations at each interval). The amount of penicillin was calculated on the basis of the highest dilution of aqueous and vitreous which inhibited the growth of test cultures in accordance with a previously reported technic.<sup>4</sup> For the determination of sulfacetamide, the fluids were withdrawn after twelve, thirty-six and seventy-two hours. Sulfacetamide was estimated according to the colorimetric method of Bratton and Marshall.<sup>10</sup>

A simple test demonstrated the location and gross distribution of the penicillin in the vitreous six hours after the intravitreal injection. The eyes were enucleated and frozen with a solid carbon dioxide mixture. They were then dissected in the vertical meridian, and the characteristic yellow pigment accompanying penicillin was visible and easily identified with ultraviolet light.

**Results**—Figure 1 shows that after six hours the average level of penicillin in the vitreous was 360 micrograms per cubic centimeter. The indi-

vidual figures varied from 180 to 480 micrograms per cubic centimeter. Examination of the frozen eyes at this interval showed an uneven distribution of the yellow pigment and its limitation to about one third of the vitreous space. This observation accounts for the variations in the individual experiments. The average concentration of penicillin after twelve hours was 58 micrograms per cubic centimeter, with the individual figures in comparative agreement (45 to 67.5 micrograms per cubic centimeter). After twenty-four hours the average concentration was 4.5 micrograms per cubic centimeter, with the individual values, again, within close range of each other. This amount was almost five times as great as that necessary to inhibit the growth of the test culture. The aqueous did not exert any antibacterial activity six, twelve and twenty-four hours after the intravitreal injection of the penicillin except in one sample, taken after six hours, in which partial inhibition of the growth of the test culture was observed in the first dilution.

The first determination of sulfacetamide was made after twelve hours. Estimations at an earlier period were omitted because of the unequal distribution of penicillin observed on gross examination of the frozen globes six hours after injection. Other determinations were carried out after thirty-six and seventy-two hours (fig 2). The average of four determinations

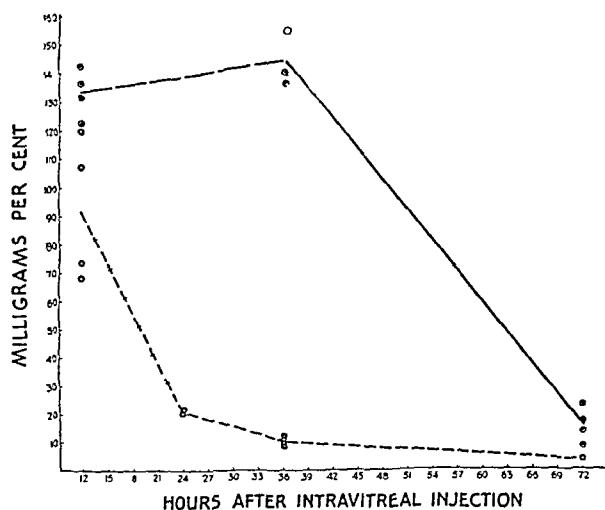


Fig 2—Concentration of sulfacetamide in the aqueous and vitreous of rabbits after a single intravitreal injection of 0.2 cc of a 10 per cent solution of sodium sulfacetamide. Values for the vitreous are shown by a solid line, and those for the aqueous, by a broken line.

after twelve hours was 133.4 mg per hundred cubic centimeters, 10.9 mg per hundred cubic centimeters less than the average value after thirty-six hours. The apparent increase in the concentration of sulfacetamide after thirty-six hours is, again, best explained by its incomplete

<sup>10</sup> Bratton, A. C., and Marshall, E. K., Jr. A Coupling Component for Sulfanilamide Determination, *J. Biol. Chem.* **128**: 537, 1939.

diffusion into all parts of the vitreous. After seventy-two hours the average concentration was 15.3 mg per hundred cubic centimeters. The amount of the sulfonamide compound in the aqueous decreased constantly from 92.2 mg per hundred cubic centimeters, after twelve hours, to 3.3 mg per hundred cubic centimeters, after seventy-two hours.

*Comment*—Comparatively little is known in regard to the length of time a drug remains in the eye after its introduction into the vitreous. Traces of fluorescein were still visible one week after a 20 per cent solution was injected into the vitreous.<sup>11</sup> It can be assumed that the molecular size of the injected compound<sup>12</sup> and the irritation produced by it are the main factors which govern the rapidity of absorption of the compounds. Also of importance are the binding of the drug to proteins, its osmotic concentration and its distribution between the aqueous phase and cells. Sulfonamide compounds are bound to plasma proteins in varying proportions, and the relative concentration of the drug in the ocular fluids depends on the amount of protein present. Since sulfacetamide usually caused great irritation, its high concentration for three days following its injection may be related to the accompanying increase in the protein to which it was bound. Penicillin was present in the vitreous in amounts considerably higher than the bacteriostatic level for more than twenty-four hours, and sulfacetamide, for more than seventy-two hours. The delayed resorption of penicillin from the vitreous space compares well with the results for the spinal fluid and for the exudate of the pleura and joints after injection into the respective closed cavities.<sup>13</sup> This observation is of foremost interest in the evaluation of intravitreal injection as a therapeutic procedure.

## II IRRITATION AND DAMAGE AFTER INTRA-VITREAL INJECTION OF ISOTONIC SOLUTION OF SODIUM CHLORIDE, PENICILLIN AND SULFACETIMIDE

Experiments were conducted to study the effects of one and two injections of penicillin within twenty-four hours. Relatively crude preparations of penicillin of medium potency

and of a purity similar to that of commercial clinical preparations were compared in their effect with purified fractions of high potency. Experiments were made to observe the effect of a single injection of sulfacetamide.<sup>8</sup> Control experiments consisted of the intravitreal injection of isotonic solution of sodium chloride. The irritation or damage was studied clinically with the slit lamp and the ophthalmoscope, histologically by various staining methods and chemically by determinations of the protein content of the aqueous.

*Technic*—The technic of injection was the same as that described in the experiments on distribution. Examinations with the slit lamp, carried out at regular intervals, included the inspection of the lens and the anterior part of the vitreous. The deeper parts of the vitreous and the fundus were examined repeatedly with the ophthalmoscope after dilation of the pupil. Histologic examinations were made of pyroxylin sections of the globes in which penicillin had been injected. Most of these eyeballs were fixed in Zenker's solution and the sections stained with hematoxylin and eosin and by the Van Gieson technic and the Weigert method for myelin sheaths. In 8 instances calottes were cut while the eyeballs were frozen, and one part was fixed in alcohol for staining of the Nissl bodies. The protein content of the aqueous was estimated as an indication of the pharmacotoxic action of the compounds on the intraocular capillaries. The determinations were made by a modification of the Looney-Walsh nephelometric method<sup>14</sup> or by the micro-Kjeldahl technic three days after the intravitreal injection of 0.2 cc of solutions containing 0.9 per cent sodium chloride, 10 per cent sodium sulfacetamide and 0.25 per cent sodium penicillin respectively. The results were correlated with the observations made with the slit lamp and the ophthalmoscope.

*Results*—Injection of 0.9 per Cent Sodium Chloride. The irritation observed with the slit lamp and the ophthalmoscope was moderate at all intervals after the injection. Remnants of fibrinous exudate, caused by the mechanical trauma, were occasionally seen in the first few days. A slight flare was sometimes noticed, but almost no cells were present. The vitreous appeared clear except for crystal-like particles behind the lens, which did not interfere with the transparency. No changes in the fundus were noted. After two weeks all signs of irritation disappeared except for a small number of glistening, brown particles in the vitreous. The protein content of the normal aqueous of rabbits ranges from 19 to 51 mg per hundred cubic centimeters.<sup>15</sup> The average protein concentration of

11 Scholer, H., and Uthoff, W. Das Fluorescein in seiner Bedeutung für den Flüssigkeits-Wechsel des Auges, in Scholer, H. Jahresberichte über die Wirksamkeit der (früher Ewers'schen) Augen-Klinik, Berlin, H. Peters, 1881, abstracted, Jahresb u d Leistung d Ophth **13** 91, 1882.

12 Penicillin has a molecular weight of about 300, and sodium sulfacetamide, a molecular weight of 222.

13 Rammelkamp, C., and Keefer, C. The Absorption, Excretion and Distribution of Penicillin, J Clin Investigation **22** 425, 1943.

14 Looney, J. M., and Walsh, A. I. The Determination of Spinal Fluid Protein with the Photoelectric Colorimeter, J Biol Chem **127** 117, 1939.

15 Ayo, C., and Meyer, K. Protein Content of Rabbits' Aqueous Humor Following Intravenous Injection of E. Coli Toxin, Proc Soc Exper Biol & Med **51** 130, 1942.



the aqueous three days after the intravitreal injection of isotonic solution of sodium chloride was 183.2 mg per hundred cubic centimeters. The difference is indicative of the increase in protein which may be ascribed to the post-traumatic irritation (table 1).

TABLE 1—*Protein Content of the Aqueous of Rabbits, Expressed in Milligrams per Hundred Cubic Centimeters, Seventy-Two Hours (Four Determinations) After the Intravitreal Injection of 0.2 cc of*

Sodium Chloride, 0.9 %	Sodium Penicillin, 2.5 %	Sodium Sulfacetamide 10 %
115	149	265
117	225	688
234	257	1,540
279	327	3,640
Average 183.2	247	1,533

Injection of Solution of Sodium Penicillin in Concentration of 2.5 Milligrams per Cubic Centimeter. After one injection of a purified fraction of penicillin (11 eyes), the signs of irritation as observed with the slit lamp and the

of the vitreous. The vitreous was not detached, but the extent of its destruction could not be established because of the fixation. The nature of the crystalline deposits behind the lens, which were visible with the slit lamp, could not be identified with the microscope, although amorphous granular debris in this area probably represents their histologic substrate. The lens and uvea appeared normal except in 2 eyes, which displayed loss of the fibrillar structure in a localized part of the subcapsular cortical layers near the posterior pole of the lens (table 2). Examination at later periods (2 eyes after two weeks, 4 eyes after four weeks) revealed a similar mild inflammatory reaction. In 7 instances the retina was free of pathologic changes. No evidences of degeneration of the Nissl bodies or of the nuclei of the ganglion cells were revealed by the Nissl stain. Gross changes of the medullated nerve fibers were not demonstrated by the Weigert stain for myelin, but finer lesions cannot be recognized with this method. The visual cells and pigment epithelium appeared normal. On the other hand, in 4 eyes circumscribed areas

TABLE 2—*Damage to Lens, Vitreous and Retina After Injections of Penicillin into the Vitreous of Normal Eyes*

Type of Penicillin Preparation	Number of Injections of Penicillin	Number of Eyes	Lens		Vitreous		Retina		
			Clear	Localized Posterior Cortical Cataract	Clear *	Extensive Exudate	Normal	Localized Atrophy	Extensive Destruction
Highly purified	1	11	9	2	11		7	4	
	2	3	1	2	2	1		1	2
Less purified	1	2		2	2			2	
	2	5	1	4	1	4		2	3

\* No or few inflammatory cells

ophthalmoscope differed from those with the isotonic solution of sodium chloride in a moderate increase of the flare and in the presence of a few cells circulating in the aqueous. A slight opacity, in the form of a veil or a small cloud, was present in the vitreous, in addition to crystalline deposits in the anterior layers which resembled those after injection of the sodium chloride solution. The opacity was usually resorbed within a short period, and the number of crystalline deposits was greatly reduced in two months. As a rule, the ophthalmoscopic examination revealed a normal fundus, especially a normal appearance of the fine striations of the medullated nerve fibers.

From 149 to 327 mg per hundred cubic centimeters of protein was present in the aqueous of 4 eyes three days after the injection of purified penicillin (table 1). Histologic examination of 2 eyes removed five days after the injection revealed a moderate number of cells, mostly round cells, in the anterior and posterior border layers

of 1 or 2 disk diameters presented different degrees of atrophy of the retina, beginning with granular disintegration of the outer segment of the rods and advancing to changes in chromatin of the outer nuclear layer and, finally, to rarefaction of all cellular elements and their replacement by glial elements. The pigment epithelium was involved secondarily.

A single injection of a crude preparation of penicillin (2 eyes) caused slightly greater irritation than that of a purified fraction of penicillin. This was evidenced by an increased flare and a greater number of cells in the anterior chamber and by the larger amount of opacities in the vitreous. These changes regressed and disappeared within two to four weeks. Crystalline deposits, similar to those observed after the injection of a purified preparation, were present behind the lens. In the examination with the ophthalmoscope the medullated nerve fibers appeared to have lost parts of the finer striations in some instances, and the area of the medullated

nerve fibers was reduced. Histologic examination of the eyes enucleated four weeks after the injection confirmed the presence of a more extensive damage to the retina. In 1 instance a flat, localized detachment of the retina was seen, with a small amount of subretinal fluid, which was rich in protein. The outer segments of the rods were broken into a mass of pale-staining granules intermingled with large droplets, which may have been secreted by the pigment epithelium.<sup>16</sup> In a number of places the cells of the pigment epithelium showed exfoliation, proliferation and the common variety of degenerative changes with which the epithelium responds to damage of the rods and cones. In addition to the histologic changes in the retina, the lens presented lesions in the posterior subcapsular layer, which were not clearly seen with the slit lamp. The fibers were swollen and club shaped near the posterior pole, and few epithelial cells were visible in this area. The vortex of the lens did not show pathologic changes.

The damage was greatly increased when a second injection of either preparation was made after twenty-four hours (8 eyes). The Tyndall sign became much more intensive and the cells more numerous. The extensive exudate in the vitreous caused a diffuse opacity, which made examination of the fundus impossible. After four weeks the condition improved, but opacities in the vitreous were still present in considerable numbers. A severe intravitreal hemorrhage occurred in a rabbit which moved unexpectedly during the procedure of injection. With the slit lamp a diagnosis was made in most instances of a slight opacity in the posterior cortex of the lens. In a few instances examination of the fundus became possible after partial resorption of the exudate and revealed small hemorrhages near the optic nerve, a flat retinal detachment and reduction of the medullated nerve fiber area, suggestive of partial atrophy. The irritation of the eye in this series of experiments was so obvious that determinations of protein in the aqueous did not seem necessary. The histologic examination confirmed and amplified the clinical findings. The cataractous changes, although limited to the superficial cortical layers at the posterior pole, were more advanced than those after a single injection. In the vitreous, remnants of exudate showing signs of organization were occasionally anchored on or around the disk. The traction they exerted may have been the cause of retinal detachment in 3 eyes, but more frequently a flat retinal detachment of the exudative

type occurred, with partial decomposition of the outer segments of the rods and cones. The circumscribed area of retinal atrophy described as an occasional lesion in the eyes which received one injection was constant and more extensive in the eyes which received two injections. The intraocular hemorrhage in the cited case extended to the retroretinal space and caused extensive total detachment with vast destruction of the retina.

**Injection of 10 per Cent Sodium Sulfacetimide.** A single injection of a 10 per cent solution of sodium sulfacetimide was followed in the first three days by an inflammatory reaction, which usually exceeded that after a single injection of penicillin. The flare in the anterior chamber was more pronounced and lasted several weeks. The cells were numerous and formed a carpet-like layer on the anterior surface of the lens within the pupil. Crystalline deposits were present in the anterior layers of the vitreous, and a moderate number of opacities in the vitreous were seen for a few days. In 1 out of 10 eyes the fundus displayed a grayish area of about 2 disk diameters, which probably represented edema. No other changes of the fundus were noticed. Four determinations of the protein content of the aqueous three days after the intravitreal injection showed an average concentration of 1,533 mg per hundred cubic centimeters, with a range of from 265 to 3,640 mg per hundred cubic centimeters (table 1). Histologic examinations were not made.

*Comment*—The injection of the newer chemotherapeutic agents into the vitreous was based on their high potency and low tissue toxicity, the latter factor distinguishing them from most other antibacterial drugs which are protoplasmic poisons. Comprehensive studies on cells and tissue cultures, that is, leukocytes, fibroblasts, epithelial tissue and microphages, were reported by Abraham and his co-workers.<sup>17</sup> Penicillin was found to be less toxic than sulfonamide compounds to leukocytes in vitro, and both were considerably less toxic than the flavines. Experiments on various laboratory animals (mice, guinea pigs and rabbits) showed the low acute toxicity of penicillin,<sup>18</sup> the toxicity being highest with fractions containing the more pigmented and less acidic components.

The studies on intravitreal injection were further encouraged by the tolerance of the vulnerable nervous system to high levels of peni-

<sup>16</sup> Koyanagi, Y, and Kinnikawa, C. Gleichwertige Veränderungen des retinalen Pigmentepithels und des renalen Tubulusepithels bei verschiedenen Vergiftungen, Arch f Ophth 137 261, 1937

<sup>17</sup> Abraham, E. P., Chain, E., Fletcher, C. M., Gardner, A. D., Heatley, N. G., Jennings, M. A., and Florey, H. W. Further Observations on Penicillin, Lancet 2 177, 1941

<sup>18</sup> (a) Fleming, A. The Antibacterial Action of Cultures of a Penicillium, with Special Reference to

cillin and by the introduction and maintenance of high concentrations in closed body cavities without untoward effects<sup>15</sup> The toxic action of injections of penicillin on subcutaneous tissue and adjacent voluntary muscles was studied by Hamre and her associates,<sup>18f</sup> who described edema and infiltration with monocytes and polymorphonuclear leukocytes in the subcutaneous tissue and destruction, infiltration and phagocytosis of the muscle fibers Selbie and McIntosh<sup>18g</sup> showed that intramuscular injections of penicillin in mice caused a relatively slight degree of muscle necrosis as compared with other chemotherapeutic drugs Although these experiments were not closely related to the studies on the eye, they pointed to the necessity for careful investigation of the effect of intravitreal injections on the delicate ocular structures

Only 1 case has been reported in which one of the newer antibacterial drugs was introduced directly into the eye, Igersheimer<sup>19</sup> injected sulfanilamide into the anterior chamber of an eye with post-traumatic iridocyclitis, with an extremely good result The effect on rabbits of intravitreal injections of a solution of sodium chloride to replace aspirated vitreous was studied by Lowenstein and Samuels<sup>2</sup> Elschmig<sup>1</sup> and later Zur Nedden,<sup>3</sup> applied this treatment with some modifications to human eyes with hemorrhages and infections of the vitreous The trauma of the injection was well tolerated despite the large size of the needle necessary for this procedure In the experiments reported here the use of a large needle was avoided in reducing the content of the eye by withdrawal of aqueous instead of vitreous fluid The use of a 0.25 per cent solution of sodium penicillin was based on previous experiments on the anterior segment of the eye<sup>4</sup>, a 10 per cent solution of sodium sulfacetamide was selected in

view of the studies of Robson and Scott<sup>20</sup> on experimental infections of the cornea Further experiments will demonstrate the extent to which the dose may be reduced to keep damage at a minimum without an essential curtailment of the therapeutic effect As the experiments so far reported were made on the eyes of rabbits and present only the initial approach to a study of intensive local treatment of acute infections of the vitreous, modifications in technic may be necessary for application to the human eye

The structures of the eye which showed signs of damage attributable to the intravitreal injection were the vitreous, the lens and the retina The slight opacities in the vitreous visible after a single injection of the purified preparation of penicillin were resorbed within a few days to two weeks They were somewhat more extensive and numerous when the cruder preparation was used A second injection, given twenty-four hours after the first, caused heavy exudation into the vitreous, this exudate occasionally became organized and led to retinal detachment The crystalline deposits seen in the anterior layers of the vitreous after injection of penicillin and sulfacetamide, as well as in the control eyes, were similar to the glistening deposits described by Lowenstein and Samuels,<sup>2</sup> who concluded that they were particles of destroyed vitreous framework These changes may be disregarded as they did not interfere with the transparency of the vitreous and showed a tendency to resorb

A single injection of the purified preparation of penicillin did not cause any detectable damage to the lens, the rupture of the lens capsule at the posterior pole on fixation with Zenker's solution and on dehydration interfered, however, with a systematic histologic study<sup>21</sup> Microscopic lesions were seen in the subcapsular layer of the posterior cortex in several eyes which had been given one injection of a crude preparation Almost all eyes with two injections of either preparation displayed early stages of a posterior cortical cataract on examination with the slit lamp The extent of the lesion may have depended on the nearness of the injected material to the posterior pole of the lens In a small percentage of all experiments the lens was injured by the needle It can be stressed, however, that the relative size of the lens and vitreous space in the human eye reduces the possibility of damage to the lens—either chemical or traumatic

Their Use in the Isolation of B. Influenzae, Brit J Exper Path **10** 226, 1929 (b) Cham, E., Florey, H. W., Gardner, A. D., Heatley, N. G., Jennings, M. A., Orr-Ewing, J., and Sanders, A. G. Penicillin as a Chemotherapeutic Agent, Lancet **2** 226, 1940 (c) McKee, C., and Rake, G. Biological Experiments with Penicillin, J Bact **43** 645, 1942 (d) Florey, H. W., and Jennings, M. A. Some Biological Properties of Highly Purified Penicillin, Brit J Exper Path **23** 120, 1942 (e) Robinson, H. J. Toxicity and Efficacy of Penicillin, J Pharmacol & Exper Therap **77** 70, 1943 (f) Hamre, D., Rake, G., McKee, C., and MacPhillamy, H. The Toxicity of Penicillin as Prepared for Clinical Use, Am J M Sc **206** 642, 1943 (g) Selbie, F. R., and McIntosh, J. The Action of Chemotherapeutic Drugs (Including Proflavine) and Excipients on Healthy Tissue, J Path & Bact **55** 477, 1943 (h) Abraham and others<sup>17</sup>

19 Igersheimer, J. Intraocular Injection of Sulfanilamide in a Case of Purulent Iridocyclitis, Am J Ophth **26** 1045, 1943

20 Robson and Scott (footnotes 9a and b)

21 von Hippel, E. Ueber verschiedene Formen von angeborener Cataract und ihre Beziehung zueinander, Arch f Ophth **54** 48, 1902

Great care was exercised in the study of possible damage to the retina in view of the sensitivity of its cellular elements. In general, the different methods of examination revealed no toxic action due to a single injection of the purified fraction of penicillin except for circumscribed lesions in a few eyes, apparently caused by the unequally distributed drug. The solution may have remained in contact with the retina in relatively high concentration for several hours because of the slow diffusion within the vitreous gel and may have caused the damage characterized by degeneration of the visual cells. Here, again, the anatomy of the human eye will probably safeguard the retina, since the point of the needle can be placed at some distance from it. The volume of the vitreous of the human eye measures about 4 cc and is about three-fifths the total volume of the globe, whereas in rabbits the volume of the vitreous is 1 to 1.5 cc and is approximately three-tenths the total volume of the globe.

Injection of a crude preparation, especially the repetition of the injection after twenty-four hours, increased the inflammatory reaction. Greater irritation was expected from the use of a relatively crude fraction in view of the increase in general toxicity with unpurified penicillin.<sup>22</sup> Much more extensive damage to the retina was produced by two injections than by one injection of either preparation. The danger of causing a retinal detachment by mechanical trauma may be ignored in view of the experiments reported here and those of Lowenstein and Samuels<sup>2</sup> and in view of the clinical observations of Elschmig,<sup>1</sup> Zur Nedden<sup>3</sup> and others. The use of a fine needle makes the procedure less objectionable and less likely to cause an intravitreal hemorrhage than the clinically accredited method for withdrawal and replacement of the vitreous. In conclusion, in consideration of the unfavorable prognosis in cases of exogenous infection of the vitreous, a single injection with a solution of purified penicillin may be regarded as a reasonably safe therapeutic procedure, especially when the injection is placed in the central portion of the vitreous.

### III EFFECT OF INTRAVITREAL INJECTION OF PENICILLIN AND SULFACETIMIDE ON EXPERIMENTAL STAPHYLOCOCCIC INFECTION OF THE VITREOUS

Pneumococcic infections are more frequent than staphylococcic infections in cases of perforating injury of the human eye. In rabbits,

however, the former often caused a septicemia which originated from the untreated control eye. Therefore, a staphylococcic infection of the vitreous was selected as the test object for treatment. A hemolytic, mannitol-positive strain of *Staphylococcus aureus*, isolated from a culture of material taken from a destructive corneal ulcer of the human eye, was used in all experiments. The strain displayed in sensitivity tests an average susceptibility to penicillin, that is, growth of a  $10^{-2}$  dilution of a broth culture was inhibited by 0.277 microgram of the purified penicillin fraction used. *Diplococcus pneumoniae*, type III, was inhibited by 0.078 microgram of the same preparation of penicillin.

**Technic**—Five-hundredths cubic centimeter of a twenty-four hour broth culture of *Staph. aureus* in a dilution of  $10^{-1}$  or  $10^{-5}$  was injected into the vitreous, with the use of local anesthesia, without prior withdrawal of aqueous. In the first four experiments with penicillin dilution of the broth culture was  $10^{-4}$ , in all other experiments a dilution of  $10^{-5}$  was injected. In the first series of experiments treatment consisted of one or two injections of 0.2 cc of a solution containing 25 mg of sodium penicillin per cubic centimeter (2,500 Oxford units per cubic centimeter). The first injection was made at intervals of six, twelve or twenty-four hours after inoculation. In the initial experiments treatment consisted of two injections and was in several instances supplemented by corneal iontophoresis on the third day. Later, one injection was employed. In the second series of experiments 0.2 cc of a 10 per cent solution of sodium sulfacetamide was introduced six hours after inoculation with the same technic as that used in the penicillin experiments. All control eyes received 0.2 cc of a 0.9 per cent solution of sodium chloride.

The course of the inflammation and the effect of the therapy were studied regularly with the slit lamp and the ophthalmoscope. Only a limited number of koda-chromes were taken because the photographed changes in the anterior segment did not reflect the severity of the inflammatory process within the vitreous space. The eyes were generally removed after four to five weeks, at a time at which almost all the signs of endophthalmitis had subsided in the successfully treated eyes. A few eyes were enucleated at an earlier stage because of intercurrent disease or accident. Cultures were made of the heart blood when the general condition suggested septicemia. Histologic examinations were made of all treated eyes, as well as of the untreated controls. The same stains as those mentioned in part II were used.

**Results**—The infection induced with the technic described led in all instances to the development of an abscess in the vitreous and to phthisis bulbi. In some instances the course was acute, involved the anterior segment and developed into the picture of panophthalmitis with perforation, followed by extreme shrinkage of the eye. In other instances the process was limited to the structures behind the iris diaphragm, with subsequent shrinkage of the globe. The infection

<sup>22</sup> Florey and Jennings<sup>18a</sup> Robinson<sup>18c</sup> Hamre and others<sup>18f</sup>

did not cause bacteremia, all cultures of the heart blood were sterile

The effect of the penicillin therapy depended on the length of time which elapsed between the inoculation and the first treatment. In the first series of experiments broth dilutions of  $10^{-4}$  and  $10^{-5}$  were injected and six hours later one or two intravitreal injections of penicillin were given. As table 3 shows, the infections were checked in all 10 eyes regardless of the size of the inoculum or the number of injections of penicillin. The same excellent results were obtained in the second series of experiments, in which treatment

injections of sulfacetamide were made in 8 eyes six hours after inoculation. The course of the inflammation did not differ from that in the untreated control eyes except in 1 eye, in which the full development of an abscess of the vitreous was delayed for about a week. A second injection was not administered after twenty-four hours, however, because the suppurative process was obviously beyond control, in spite of the high concentration of the sulfonamide compound which persisted in the inner fluids of the eye for more than three days (part II). The complete failure of sulfacetamide

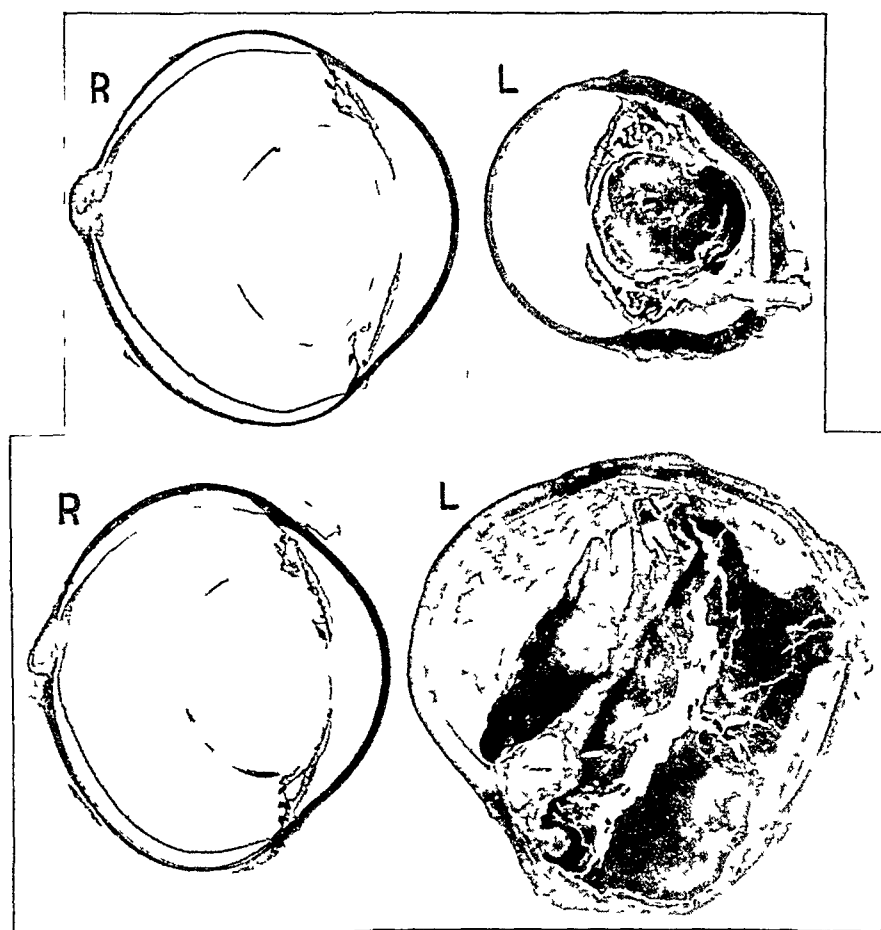


Fig 3—Sections of the treated (*R*) and untreated (*L*) eyes of 2 rabbits with staphylococcal infection of the vitreous three weeks after therapy. Treatment consisted of a single injection of 0.2 cc of a solution containing 2.5 milligrams of penicillin sodium per cubic centimeter twelve hours after inoculation with the organisms.

was initiated twelve hours after the injection of a  $10^{-5}$  dilution of *Staph aureus* (fig 3). It should be emphasized that of the 10 effectively treated eyes of this series, 6 were given only one injection of penicillin. The treatment was unable to check the infection in any of 11 eyes treated twenty-four hours after the inoculation, although a beneficial result was observed in some rabbits. The injection was not repeated because the inflammatory process was so advanced after forty-eight hours that no favorable result could be expected from further treatment.

therapy begun six hours after inoculation made experiments with a longer interval unnecessary.

Although the infections were checked in all 20 eyes treated with penicillin six and twelve hours after inoculation, various structures of the posterior segment showed certain signs of damage attributable in part to the infection and in part to the treatment. Some changes were observed by biomicroscopic and ophthalmoscopic studies, others were discovered during histologic examination. Table 4 contains a summary of the changes observed by the various methods.

of examination. Cataractous changes, suggested by slit lamp inspection and identified on histologic examination, were found in 3 eyes in the six hour series and in 6 eyes in the twelve hour experiments. Six of the eyes with a beginning complicated cataract had received two injections of penicillin. Lesions in the lens were composed of subcapsular vacuoles, irregular proliferation of pseudoepithelium on the posterior capsule of the lens and the formation of Wedl's cells. The fibrils at the posterior pole were thickened and swollen, and a fine granular debris and Morgagni spheres were seen in the most advanced cataracts. As a rule the lesions were minor and did not interfere with the visibility of the details of the fundus.

show signs of regression during the period of observation. These strands were identified under the microscope as organized remnants of cellular exudate adherent to the surface of the optic disk or the surrounding retina. The histologic examination in the earlier stages revealed an accumulation of round cells behind the lens and in other parts of the cortex of the vitreous, the exudate was necrotic in sections taken at later stages. The number of injections of penicillin was a definite factor in relation to the extent of the opacity, that is, the second injection increased greatly the inflammatory signs. The time interval between the inoculation and the treatment was of less importance.

TABLE 3—Results of Intravitreal Injection of Sodium Penicillin and Sodium Sulfacetimide at Various Intervals After Infection of the Vitreous with *Staphylococcus Aureus*

Treatment		Hours Between Infection and First Treatment	Total Number of Eyes	Number of Eyes in Which	
Drug	Number of Injections			Infection Was Checked	Infection Was Not Checked
0.25 per cent sodium penicillin	1	6	4	4	0
	2	6	6	6	0
	1	12	6	6	0
	2	12	4	4	0
	1	24	10	0	10
10% sodium sulfacetimide	1	6	8	0	8
Control eyes—0.9% sodium chloride	12	6, 12, 24	20	0	20

TABLE 4—Damage of Lens, Vitreous and Retina in the Successfully Treated Eyes with *Staphylococcus* Infection of the Vitreous Observed Three to Five Weeks After Inoculation

Number of Injections of Penicillin	Hours Between Infection and First Treatment	Number of Eyes	Lens		Vitreous		Retina		
			Clear	Localized Posterior Cortical Cataract	Clear *	Extensive Exudate	Normal	Localized Atrophy	Extensive Destruction
One	6	4	3	1	4		1	2	
	12	6	4	2	4	1	5	1	1
Two	6	6	4	2	5	1	4	1	
	12	4		4	2	2	4		1

\* No or few inflammatory cells

Changes of the vitreous consisted of fine deposits which resembled scintillatio and which diminished greatly in number during the period of observation of two months. They were mostly iridescent and transparent, sometimes opaque white and occasionally pigmented. Like the opacities in the lens, they did not interfere with the ophthalmoscopic examination of the eye-ground. The second type of change in the vitreous was seen as clouds of opacities of varying density, which prevented the examination of the fundus for the first few weeks. After they had cleared in part, a circumscribed opaque mass was frequently visible in the lower peripheral portion of the vitreous and was generally resorbed in the following weeks. In 3 eyes dense strands were formed, however, which did not

Local areas of retinal atrophy, the size of about 1 disk diameter, were observed in a few eyes. Since they were similar to areas noted after the injection of penicillin without infection, they probably were caused by the proximity of the penicillin depot to the retina. In other eyes the residue of cellular exudate on the surface of the retina had produced proliferation of the neuroglia, followed by atrophy of the retina. Traumatic damage of the retina by the needle was found in 2 eyes and consisted of tears and a circumscribed retinal detachment. A flat, localized retinal detachment around the optic nerve in 2 eyes was attributed to the treatment with two injections. The uvea was normal except in 2 eyes, in which scattered foci were seen in the choroid.

*Comment*—The experiments on the therapeutic effect of intravitreal injections of penicillin and sulfacetimide were limited to an exogenous infection with a mannitol-positive strain of *Staph aureus* of average susceptibility to penicillin. No systemic therapy was applied because of the almost complete failure of the oral administration of sulfadiazine in treatment of various experimental exogenous infections of the anterior segment of the eye<sup>23</sup> and because of the unavailability of penicillin in the quantity necessary for systemic therapy.

Consistent standard lesions were obtained with the technic described. All the control eyes were lost, although the inflammation sometimes ran a fulminant course and sometimes developed gradually (four to seven days) to the clinical picture of an abscess of the vitreous.

The extremely favorable results of penicillin treatment begun within twelve to thirteen hours after inoculation are clearcut, since, without exception, all eyes were saved. The larger inoculum which was injected in four of the six hour experiments did not change the effect of the treatment. A single injection of the solution of penicillin was as beneficial as two injections followed by iontophoretic treatment of the anterior segment and caused considerably less reaction.

The treatment failed almost completely with an interval of twenty-four hours between inoculation and the first injection.

Untreated eyes removed thirty hours after infection showed histologically dense leukocytic infiltration and disarrangement of the retina, as well as an exudative retinal detachment. The extensive destruction in this brief period is certainly a factor in the inefficacy of local penicillin treatment begun twenty-four hours after inoculation. It cannot be decided from these experiments with acute infections, however, whether the active maturation of the bacteria also played a part, as may be expected in view of the in vitro experiments of Hobby and her co-workers.<sup>24</sup>

A purified penicillin preparation of high potency was used in all experiments because of its lower toxicity as compared with crude preparations. Although infections with only one strain of *Staph aureus* were studied, there is a good basis for the prediction of a similar

effectiveness of early penicillin therapy of exogenous infections of the vitreous with other organisms susceptible to the inhibitory action of penicillin. Since most strains of *Staph aureus*, hemolytic streptococcus and *D pneumoniae* are highly sensitive to the antibacterial activity of penicillin, a large majority of the exogenous intraocular infections present a promising field for local penicillin therapy.

Disappointing results with intravitreal injection of a 10 per cent solution of sodium sulfacetimide were obtained with infections with only one strain of *Staph aureus*. No general conclusions should be drawn, therefore, in regard to the efficacy of the treatment for infections with other strains. The inflammatory reaction following the injection of this solution was, on the other hand, considerably greater than that after the injections of penicillin, and more caution would be required in its use.

It may be concluded from this experimental study that a single intravitreal injection of a purified potent penicillin is a reasonably safe procedure and that its application is justified in treatment of exogenous infections of the vitreous. The use of supplementary treatment, such as mydriatics, heat or fever or shock therapy, is advised in cases of infections of the vitreous of the human eye in order to increase the cellular and humoral body defenses, to hasten the resorption of the exudate and to prevent complications. The combination with immunotherapy, as pointed out by Thygeson,<sup>25</sup> may be useful with some infections. When the anterior segment is also involved, iontophoresis with penicillin can be combined with intravitreal injection of the drug. Systemic treatment should be added if the infective process has spread to the richly vascularized structures of the eye.

#### SUMMARY

1 A single injection of 0.2 cc of a solution containing 25 mg of sodium penicillin per cubic centimeter into the vitreous of rabbits secured a bacteriostatic activity of the vitreous fluid for more than twenty-four hours.

2 A single injection of 0.2 cc of a 10 per cent solution of sodium sulfacetimide led to a high concentration of the sulfonamide compound in the vitreous and a lower concentration in the aqueous. The level of the substance in the vitreous was found to be close to 15 mg per hundred cubic centimeters seventy-two hours after the injection.

23 von Sallmann L. Penicillin and Sulfadiazine in the Treatment of Experimental Intraocular Infections with *Staphylococcus Aureus* and *Clostridium Welchii*, *Arch Ophth* 31:54 (Jan) 1944, footnote 4.

24 Hobby, G., Meyer, K., and Chaffee, E. Observations on the Mechanism of Action of Penicillin, *Proc Soc Exper Biol & Med* 50:281, 1942. von Sallmann 4.

25 Thygeson, P. Sulfonamide Compounds in Treatment of Ocular Infections, *Arch Ophth* 29:1000 (June) 1943.



3 The damage to the inner structures of the eye attributable to the injected purified preparation of penicillin was limited in general to a slight inflammatory reaction, without integral lesions of the retina, lens or vitreous. In several instances, however, circumscribed atrophy of the retina was noted, probably caused by the proximity of the penicillin depot. The lesions were more pronounced on injection of a relatively crude preparation of penicillin.

4 The damage produced by repeated intravitreal injection was considerable and consisted occasionally of permanent lesions of the retina or the lens.

5 The irritation following the injection of sulfacetamide was usually greater and more pro-

longed than that following the injection of penicillin.

6 A reliable standard infection of the vitreous leading to phthisis bulbi was produced by the intravitreal injection of 0.05 cc of a broth culture of *Staph aureus* in a dilution of  $10^5$ .

7 The infection was checked in all instances by penicillin when it was injected into the vitreous six or twelve hours after the inoculation. The treatment was only of slight benefit when initiated twenty-four hours after inoculation.

8 The infection was not influenced by the intravitreal injection of sodium sulfacetamide administered six hours after the inoculation.

Miss C. Zink did most of the histologic technique.

630 West One Hundred and Sixty-Eighth Street



# SIMULTANEOUS LOCAL APPLICATION OF PENICILLIN AND SULFACETIMIDE

LUDWIG VON SALLMANN, M D

WITH THE TECHNICAL ASSISTANCE OF J. FANTLE DI GRANDI  
NEW YORK

Many species of bacteria pathogenic to the eye are susceptible to the newer chemotherapeutic agents—both to sulfonamide compounds and to the products of molds, a few (*Bacillus pyocyaneus*, Morax-Axenfeld diplobacillus, *Haemophilus influenzae* and Friedlander's bacillus) are susceptible only to sulfonamide compounds. The degree of sensitivity of the species of the infecting organism to the drugs is but one of a number of factors which influence the therapeutic result. Also of importance are initial differences in sensitivity of strains of the same species to the selected compound and subsequent differences developing during the period of treatment, due in part to the maturation of the bacteria. Other factors are the number and the virulence of the infecting organisms, the amount of protein breakdown products or pus and the quality of the cellular and humoral body defenses. Some of these factors cannot be evaluated at all, and others require time-consuming tests. In view of the many unknown factors and because of the difference in the mechanism of the antibacterial action of sulfonamide compounds and that of mold products, a study of a combined local treatment with penicillin, as the most promising mold product, and a sulfonamide compound was indicated. The conditions present in acute intraocular infections suggest the usefulness of such a treatment, inasmuch as the bacteriologic diagnosis is frequently uncertain and the prognosis unfavorable in the event of a delay in the treatment.

## EXPERIMENTAL STUDY

Preliminary experiments were related to the compatibility of penicillin and sulfonamide compounds in vitro, and specifically to the effect of the sulfonamide compounds on the bacteriostatic action of the labile penicillin. The activity of

the penicillin<sup>1</sup> was determined according to the dilution method of Fleming<sup>2</sup>, an eighteen hour broth culture of *Diplococcus pneumoniae*, type III, in 10<sup>-1</sup> dilution was used as the test culture. Appropriate dilutions of penicillin were made in parallel series, and to each tube was added an equal amount of the test culture. After incubation at 37 C for twenty-four hours, the tubes were examined for inhibition of growth of the culture, and the amount of penicillin was calculated on the basis of the highest dilution in which growth was inhibited. To each tube of another parallel series was added sodium sulfadiazine in concentrations of 1, 1,000 to 1, 10,000. It was found that in all series growth of the culture was inhibited by 0.25 micrograms per cubic centimeter of the penicillin preparation used. The addition of sulfadiazine did not have any antagonistic effect on the inhibitory activity of the penicillin. In further in vitro experiments, sodium sulfacetimide was added in a concentration of 5 per cent to the usual solution containing 0.25 microgram per cubic centimeter of sodium penicillin, and no difference was noted in the antibacterial action of the penicillin. The effects of penicillin on the antibacterial action of sulfonamide compounds was not examined in this study, since the experiments of Hobby<sup>3</sup> have shown that penicillin does not exert an anti-sulfonamide action.

The next part of the study was concerned with the iontophoretic application to rabbits' eyes of a solution containing penicillin and a sulfonamide compound and the quantitative determination of these substances in the aqueous. Morisot,<sup>4</sup> Erlanger<sup>5</sup>, Brecher<sup>6</sup> and others recommended

1 The penicillin was extracted and prepared in the laboratory of Dr. Karl Meyer.

2 Fleming, A. In-Vitro Tests of Penicillin Potency, *Lancet* **1** 732, 1942.

3 Hobby. Personal communication to the author.

4 Morisot. Iontotherapie en therapeutique oculaire, *Clin. opht.* **32** 77 and 499, 1928.

5 Erlanger, G., and Erlanger, A. Behandlung der Lederhautentzündung mit Calcium-Adrenalin bzw. Histamin-Iontophorese, *Klin. Monatsbl. f. Augenh.* **88** 93, 1932. Erlanger, G. Elektrische Einverleibung von Pharmaka ins Auge, *Jahresk. f. ärztl. Fortbild.* **23** 22, 1932.

(Footnote continued on next page)

This study was supported by the Knapp Memorial Foundation.

Read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, March 20, 1944.

From the Department of Ophthalmology of Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology of Presbyterian Hospital.

the simultaneous iontophoretic introduction of two or more isotropes into the eye, but to my knowledge no quantitative estimations were made to establish the rationale of the procedure. In the present experiments a solution containing 25 mg per cubic centimeter of sodium penicillin<sup>7</sup> and 5 per cent sodium sulfadiazine was applied for five minutes at 2 milliamperes, with the use of local anesthesia induced with nupercaine hydrochloride. After one hour the aqueous was withdrawn from the identically treated eyes of single

TABLE 1—Activity of Penicillin and Concentrations of Sulfacetimide in the Aqueous of Rabbits Forty-Five to Sixty Minutes After the Iontophoretic Application of Sodium Penicillin, Sodium Sulfacetimide and a Solution of Both

Iontophoretic Application of	Activity of Penicillin, Expressed in Terms of Dilution of Aqueous Able to Inhibit Growth of <i>D. Pneumoniae</i> , III, 10 <sup>-1</sup>	Concentration of Sulfacetimide in Aqueous, Mg/100 Cc
Sodium penicillin, 25 mg/cc	1/64 1/64 1/64 Average, 1/64	
5% sodium sulfacetimide		35.2 29.7 46.9 48.4 Average, 40.1
Solution containing 25 mg/cc of sodium penicillin and 5% sodium sulfacetimide	1/48 1/64 1/64 1/44 Average, 1/55	36.0 42.6 35.9 52.5 Average 41.8

\* Each solution was applied for five minutes with a current of 2 milliamperes. Local anesthesia was induced with nupercaine hydrochloride.

rabbits and pooled. Two-tenths cubic centimeter was used in each of two parallel series for the calculation of penicillin according to activity tests. The remainder was used for the colorimetric determination of the sulfonamide compound according to the method of Bratton and Marshall<sup>8</sup>.

The concentration in the aqueous after the iontophoretic application of the solution containing the two compounds was compared with the concentrations obtained with a solution of sodium penicillin alone, sodium sulfacetimide alone and sodium sulfadiazine alone,<sup>9</sup> introduced by a similar technic. As table 1 shows, the concentrations

after the simultaneous introduction of penicillin and sulfacetimide approach those found in the aqueous after iontophoresis of a simple solution of penicillin or of sulfacetimide. The slight differences of the relative figures are within the limits of error of the quantitative methods. On the other hand, the figures for the concentration of sulfadiazine in the aqueous (not given in the table) after the application of a solution containing the sodium salts of sulfadiazine and of penicillin were significantly lower (25 mg per hundred cubic centimeters) than the values after the application of sodium sulfadiazine alone (more than 40 mg per hundred cubic centimeters). The explanation for the difference is seen in the precipitation of the free sulfadiazine acid at the  $p_H$  of the solution of sodium penicillin.

The eyes, especially the corneas, of the rabbits were examined for signs of irritation or damage which could be attributed to the application of the mixture. A transient haze of the corneal epithelium was frequently present—similar to that seen after the application of penicillin alone.<sup>10</sup> Human eyes with intraocular infections were also treated with a mixture of sodium penicillin and sodium sulfacetimide for five minutes at 2 milliamperes at intervals of twenty-four hours over a period of three to five days, without untoward effect.

TABLE 2—Results of Penicillin, Sulfadiazine and Penicillin-Sulfacetimide Treatment, Beginning Six Hours After Injection of a 10<sup>-4</sup> Dilution of *Staph. Aureus* into the Anterior Chamber, with Simultaneous Injury of the Lens

Treatment	No. of Eyes	Recoveries	Losses
Sodium penicillin iontophoresis	12	9	3
Sodium sulfadiazine iontophoresis and oral use of sulfadiazine	12	1	11
Sodium penicillin and sodium sulfacetimide iontophoresis and oral use of sulfadiazine	12	9	3
Control eyes—no treatment	9	0	9
Control eyes—influenced only by oral use of sulfadiazine	15	0	15

The last part of the investigation dealt with the comparative effect of three types of therapy on a staphylococcal endophthalmitis produced in chinchilla rabbits. A 10<sup>-4</sup> dilution of a twenty-four hour broth culture of a mannitol-positive *Staphylococcus aureus* was used, and 0.05 cc was injected into the anterior chamber after extensive damage to the lens with the needle. The three types of therapy, applied six hours after the inoculation and repeated over a period

6 Brecher, I. Ueber eine neue kombinierte Anwendungsweise der Dielektrophorese am Auge zwecks Erzielung einer wirksameren und tieferen Ionenpenetration, *Klin Monatsbl f Augenh* 97:399, 1936.

7 Although actual titrations by the Oxford method were not made, 1 cc of the solution was estimated to contain approximately 1,000 Oxford units.

8 Bratton, A. C., and Marshall, E. K., Jr. A Coupling Component for Sulfanilamide Determination, *J Biol Chem* 128:537, 1939.

9 von Sallmann, L. Sulfadiazine Iontophoresis in Pseudomonas Infection of Rabbit Cornea, *Am J Ophth* 25:1292, 1942.

10 von Sallmann, L., Meyer, K., and Di Grandi, J. Penetration of Penicillin into the Eye, *Arch Ophth* 31:1 (Jan) 1944.

of five days, were as follows (1) iontophoresis with penicillin, (2) iontophoresis with sulfadiazine and oral use of sulfadiazine, and (3) iontophoresis with a mixture of the sodium salts of penicillin and sulfacetimide combined with the oral administration of sulfadiazine

The results of the various treatments are compared in table 2. Nine out of 12 eyes were saved by local penicillin therapy. The infection was checked in only 1 out of 12 eyes treated locally and systemically with sulfadiazine. The combined local treatment with penicillin and sulfacetimide, supplemented by the systemic administration of sulfadiazine, was effective in 9 out of 12 eyes.

The experiments with intraocular infections produced by one strain of *Staph aureus* showed that the efficacy of local penicillin therapy was not increased by its combination with topical application of sulfacetimide, supplemented by systemic administration of sulfadiazine. It must be emphasized, however, that there are great differences in the sensitivity of strains of *Staph aureus* to sulfonamide compounds. No general conclusions should be drawn from these experiments, therefore, in regard to infections with other strains of *Staph aureus* or with other species. More favorable response to the com-

bined treatment, exceeding that to local penicillin therapy, can certainly be expected in infections with strains of greater susceptibility to the sulfonamide compounds. In conformance with this opinion, a few patients with intraocular infection were treated in the Presbyterian Hospital. The doubtful cause of their infection and the urgency of early treatment favored the selection of this type of therapy. The number of patients is too small, however, to permit any conclusions.

#### SUMMARY

1 Sulfadiazine and sulfacetimide do not exert any noticeable antagonistic effect on the bacteriostatic activity of penicillin *in vitro*.

2 Approximately the same concentrations of penicillin and sulfacetimide are found in the aqueous of rabbits after the iontophoretic application of a solution containing both their sodium salts as after the iontophoretic application of a solution containing the respective salt.

3 Topical treatment with penicillin and sulfacetimide, supplemented by systemic administration of sulfadiazine was not more effective than local penicillin therapy in the treatment of an experimental intraocular infection with one strain of *Staph aureus*.

630 West One Hundred and Sixty-Eighth Street

# LOCAL VERSUS SYSTEMIC PENICILLIN THERAPY OF RABBIT CORNEAL ULCER PRODUCED BY GRAM-NEGATIVE ROD

IRVING H LEOPOLD, MD, DSc, LIDA F HOLMES, PhD,  
AND WILLIAM O LAMOTTE JR, MD

PHILADELPHIA

In evaluating any chemotherapeutic agent against infection *in vivo*, one has to determine the best method of administration for the anatomic site involved. In treatment of corneal infections with penicillin two main routes of administration are available, local application to the cornea and systemic administration.

Two methods of obtaining information concerning the routes of administration in experimental animals allow one to predict the results to be expected in human beings. Both methods are essential. The first is to determine the concentration reached in the cornea by the various means of administration, the second is to compare the effects of the methods against a standard lesion. No one has measured the concentration of penicillin in the cornea produced by either local or systemic use. The present biologic methods of estimating the concentration of the drug make such a determination in corneal tissue most difficult. It was our purpose in this study to compare the effect of application of local penicillin with that of intramuscular administration of the drug against a standard ocular infection. The local method chosen for this study was that of application of drops of a solution of penicillin at frequent intervals. Of the various local procedures tested by von Sallmann<sup>1</sup> for obtaining levels of penicillin in the aqueous, drop instillation gave the lowest concentration in the aqueous, therefore this method was chosen in order to make the comparison fairer. The intramuscular route of systemic administration was selected for this study because it is the most practical for systemic use.

During routine cultures of material from the cul-de-sacs of rabbit eyes a gram-negative bacillus was repeatedly obtained. When this organism, isolated in pure culture, was injected into the

rabbit cornea, a characteristic ulcerative lesion was regularly produced.

The cultural and biochemical reactions of the organism correspond in some respects to those of the Friedlander group. However, Dr Louis Juhanelle, in a detailed examination of the organism, found that it was not in the Friedlander-Klebsiella rhinoscleromatis group. As far as we have been able to determine, it is a bacterium which has not been previously described. It is a nonmotile, gram-negative rod, which forms an elevated, moist colony. Surface growths on agar may become confluent, and the condensation water of an agar slant becomes mucoid. After two or three days' growth the colonies undergo a radical change in appearance, becoming flat and dry. Dextrose, but not lactose, is fermented without gas, and nitrate is reduced. Infusion broth will not support growth of the organism unless enriched with neopeptone, or, preferably, with dextrose or lactose. A more complete description of the organism will be the subject of a future paper.

Sensitivity tests, with use of the 'well' method,<sup>2</sup> showed that this organism is sensitive to the action of penicillin but requires fifty times as much penicillin for inhibition as does a strain of *Staphylococcus aureus* of average sensitivity.

With the demonstration of sensitivity of this gram-negative organism to penicillin *in vitro*, it was desirable to determine whether the sensitivity existed *in vivo*. For these experiments it was possible to utilize the ulcerative lesion of the rabbit cornea mentioned.

## THE STANDARD OCULAR LESION

Blue-eyed chinchilla rabbits, weighing 2 to 3 Kg, were used. It was found that intracorneal injection of a diluted twenty-four hour dextrose broth culture of this organism produced a severe infiltration, with vascularization, of the cornea and hypopyon. By regulation of the number of organisms injected, lesions of varying degrees of severity could be produced. Injection of sterile dextrose broth alone in control eyes produced only an area of localized edema, which disappeared approximately forty-eight hours later.

For the experiments reported here, a twenty-four hour dextrose broth culture of the organism was diluted

2 Fleming, A. *In-Vitro Tests of Penicillin Potency*, Lancet 1 732, 1942

From the Department of Ophthalmology and the Harrison Department of Surgical Research of the University of Pennsylvania.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Pennsylvania.

1 von Sallmann, L., Meyer, K., and Di Grandi, J. Penetration of Penicillin into the Eye, Arch Ophth 31 1 (Jan) 1944

one hundred times with sterile isotonic solution of sodium chloride, and 0.02 cc of the diluted culture was injected intracorneally. Culture counts showed that this provided approximately 400 organisms per injection. Within twenty-four hours such an injection produced a localized area of corneal edema and infiltration, pericorneal injection and aqueous flare and floaters. In forty-eight hours the infiltrated area was denser and larger and the pericorneal injection greater, and pus cells began to collect in the angle of the anterior chamber. The lesion increased in severity gradually. By the sixth day large areas of the cornea were invaded by the limbal blood vessels. The invading vessels lay in the superficial stroma. By this time the hypopyon became massive, occupying the lower third of the anterior chamber, and there had already developed some loss of corneal epithelium and stroma. There was little change in the lesion up to the tenth day, then in 75 per cent of the eyes the process began to subside, so that by the end of the third week all the corneal



Standard ocular lesion, seven days old, showing hypopyon, vascularization and ulceration of the cornea

vessels had disappeared. The pericorneal injection had subsided, epithelium covered the defect in the cornea, and the area of opacification became less dense. The remaining 25 per cent of the eyes went on to perforation and loss of function. Cultures of material from the infiltrated areas taken at the end of seventy-two hours were positive for the gram-negative organism in 100 per cent of the control eyes. The figure shows a lesion as it appeared on the seventh day.

#### INFLUENCE OF PENICILLIN THERAPY

The penicillin used in these studies had a potency of approximately 200 units per milligram and was obtained from the Committee on Medical Research, through Dr Chester S. Keefer.

Fifteen rabbits were used in this series. Approximately 400 organisms (0.02 cc of a twenty-four hour culture in dextrose broth, diluted one hundred times with sterile isotonic solution of sodium chloride) was injected into the cornea of each eye. Two hours after injection the right eyes of the first 12 rabbits received

penicillin locally, the left eyes of the same 12 rabbits were given no therapy. The concentration of penicillin was 500 units per cubic centimeter. The penicillin was diluted in sterile isotonic solution of sodium chloride, and 3 drops (approximately 0.25 cc) was applied to the cornea and cul-de-sac every hour, the applications starting at 11 a. m. and continuing until 10 p. m., when therapy was stopped. Treatment was started again at 9 a. m. the next day, and the penicillin was applied every hour until 10 p. m. On the third day the penicillin was instilled only four times in twenty-four hours, and its administration was then discontinued entirely.

The remaining 3 rabbits received penicillin intramuscularly, the injections being started two hours after injection of the culture into both eyes. A dose of 250 units of penicillin per kilogram of body weight was injected into the gluteal region of each rabbit. Injections were made every two hours until 12 p. m., the treatment starting again at 8 a. m. the next morning. This therapy was continued for three days, and the injections were then reduced to one every four hours for two more days, when treatment was stopped.

All the eyes were examined daily with the aid of a biomicroscope. Material for culture was taken from all the eyes seventy-two hours after injection and then daily, at 8 a. m., after the lull in therapy.

#### RESULTS

*Experiment 1*—At the end of seventy-two hours cultures were positive for the gram-negative bacillus for all untreated eyes and for all 6 eyes of the rabbits treated by intramuscular injection. Corresponding cultures were negative for 10 of the locally treated eyes, and one colony resulted from culture of material from each of the remaining 2 eyes.

Clinically, each one of the untreated, control eyes displayed a course of events similar to that of the standard lesion. The lesions in all 6 eyes of the rabbits given intramuscular injections of penicillin followed the same course as did the standard lesion. In none of the 12 eyes treated by local instillation of penicillin did corneal infiltration, corneal vascularization, aqueous flare and floaters or corneal slough develop. At the end of twenty-four hours one could discern only the point of the needle puncture and localized edema in these eyes. In 8 eyes a minute spot or haze could still be made out with the biomicroscope at the site of injection at the end of the first week. These spots gradually reduced in size, so that they were barely perceptible, even by corneal microscope, at the end of two weeks. The corneas of the remaining 4 locally treated eyes were entirely clear by the fifth day.

*Experiment 2*—With 15 rabbits penicillin therapy was delayed twenty-four hours after injection of the culture into the cornea.

The same technic was used as in experiment 1. However, here 0.02 cc of a twenty-four hour dextrose broth culture, diluted 1:100, contained approximately 10,000 organisms. Therapy was

not started until twenty-four hours after inoculation but was applied on the same time schedule as in experiment 1. Twelve rabbit eyes received local therapy, the other eye of each rabbit acting as the control, and 3 rabbits received intramuscular therapy.

In all eyes, both treated and untreated, there had developed corneal edema, corneal infiltration, pericorneal injection and aqueous flare and floaters at the end of twenty-four hours. In seventy-two hours the lesions were pronounced. However, after seventy-two hours the locally treated eyes showed a definitely smaller area of infiltration, less corneal edema and smaller collections of cells in the anterior chamber, and in 6 of the locally treated eyes hypopyon did not develop. The cornea in all eyes was invaded by vessels, the locally treated eyes showing a smaller amount of vascularization. By the second week the locally treated eyes were distinctly better than the control eyes in that the areas of infiltration were decreased, corneal edema had largely subsided and many of the vessels were disappearing. In four weeks 10 of the untreated eyes had perforated, while all of the locally treated eyes remained intact. By this time the lesions of the locally treated eyes had subsided with large scars, the cells in the anterior chamber having been completely absorbed and the vessels having disappeared. In only 2 of the control eyes did the process subside. The process in the eyes of the rabbits treated intramuscularly ran practically the same course as did that in the control eyes, no significant difference being discernible.

#### COMMENT

The experimental data show that this gram-negative organism, obtained by routine culture of material from the conjunctival cul-de-sacs of rabbit eyes, is sensitive to penicillin *in vitro*. The experiments demonstrate that this organism can produce a corneal lesion when injected intracorneally. The development of this corneal lesion can be prevented by the use of local penicillin but not by intramuscularly administered penicillin. Once the lesion is established, local penicillin therapy benefits the course of the lesion but does not prevent the occurrence of considerable ocular damage. Intramuscularly administered penicillin does not appear to alter significantly the course of the lesion when therapy is started twenty-four hours after injection.

It is evident that longer-continued therapy might have produced better results. It is possible also that intramuscular therapy would have been successful if the treatment schedule had not been interrupted for eight hours. However, local therapy, which did benefit the lesion, was interrupted for a similar interval.

It must be stressed that this observation of the superiority of local over systemic treatment applies only to corneal infection and should not be construed to apply to infections of other ocular structures.

Attempts to improve the results by including a detergent, such as duponol ME Dry<sup>2a</sup> 0.4 per cent, in the penicillin preparations had to be discontinued because repeated application of the detergent in this concentration was damaging to the cornea.

Although, as a rule, gram-negative rods are insensitive to the action of penicillin, a few species are moderately susceptible, and still others exhibit a slight degree of sensitivity. Abraham and co-workers<sup>3</sup> showed that *Salmonella gartneri* was inhibited by a 1:20,000 dilution, and *Salmonella typhi* by a 1:10,000 dilution, of a solution of penicillin which inhibited a culture of *Staph aureus* when diluted 1:1,000,000.

In the experience of Fleming<sup>4</sup>, Hobby, Meyer and Chaffee<sup>5</sup>, McKee and Rake,<sup>6</sup> and of this laboratory, members of the Friedlander group of bacilli have been insensitive to penicillin. However, Smith<sup>7</sup> showed that variation in strains is remarkable in this group, and the sensitive strains which he encountered included some of type A. A similar situation was reported by Churchman<sup>8</sup> in that among gram-negative rods, on the whole insensitive to the action of methylosaniline chloride, an occasional sensitive strain may be encountered.

#### CONCLUSION

Local application of penicillin proved to be more effective than intramuscular administration in the treatment of corneal infections due to a gram-negative bacillus. The organism was sensitive to the drug *in vitro* and *in vivo*, as determined by the "well" method of Fleming and associates.

2a Duponol is a registered trademark designating certain higher aliphatic alcohol sulfates and their derivatives which are used as detergents. Duponol ME dry is derived from technical lauryl alcohol and contains a minimum of electrolytes.

3 Abraham, E. P., and others. Further Observations on Penicillin, *Lancet* **2** 177, 1941.

4 Fleming, A. The Antibacterial Action of Cultures of a *Penicillium*, with Special Reference to Their Use in the Isolation of B. Influenza, *Brit J Exper Path* **10** 226, 1929.

5 Hobby, G. L., Meyer, K., and Chaffee, E. Activity of Penicillin *in Vitro*, *Proc Soc Exper Biol & Med* **50** 277, 1942.

6 McKee, C. M., and Rake, G. Biological Experiments with Penicillin, *J Bact* **42** 645, 1942.

7 Smith, L. D. The Bacteriostatic Agent of *Penicillin Chrysogenum*, *J Franklin Inst* **254** 396, 1942.

8 Churchman, J. W. Further Studies on Behavior of Bacteria Toward Gentian Violet, *J Exper Med* **33** 569, 1921.

# TREATMENT OF OCULAR TUBERCULOSIS

FRANK N KNAPP, M D

DULUTH, MINN

The treatment of ocular tuberculosis perhaps dates from 1855, when, according to Duke-Elder,<sup>1</sup> Jaeger, through the use of the ophthalmoscope, observed the occurrence of choroidal foci in conjunction with milary tuberculosis. The subsequent evolution of methods of examination, in particular the inauguration of tests with tuberculin and roentgenographic examination of the intrathoracic organs, as well as the promulgation of the doctrine of immunity and the possibility of the microscopic exploration of the anterior segment of the eye in vivo with the aid of the slit lamp, devised by Gullstrand,<sup>2</sup> represented important additions to the knowledge of tuberculous diseases of the eye. Goldenburg<sup>3</sup> stated the belief that the discovery of tuberculin by Koch, in 1891, exerted a profound influence on ophthalmologic practice, although the indiscriminate application of tuberculin led to the abuse and consequent repudiation of its use.

During the past ten years notable advances have been achieved in the general therapy of tuberculous diseases of the eye, chiefly through administration of the several preparations of tuberculin now available for the purpose and through the employment of vaccines and antigens, autohemotherapy, the use of gold salts, phototherapy and the institution of sundry more or less empiric forms of treatment.

Previously, treatment with tuberculin was utilized less frequently, perhaps in consequence of the insistence on its employment only with carefully selected patients and of the restrictions in the manner and extent of its application. The scope of vaccinothrapy was amplified because it was often substituted for the more conventional methods of specific treatment. The progress of antigenic therapy, likewise, served in large measure to replace tuberculin therapy. Autohemotherapy acquired enthusiastic advocates. Although opinions concerning the value of

chrysotherapy were divided, on the whole they were favorable. Phototherapy and radiotherapy once more demonstrated their superior merit in appropriate instances. The results from various tentative procedures, as recorded, failed to afford adequate criteria for judgment of their therapeutic value.

It has been demonstrated repeatedly that the uvea constitutes a particularly favorable nidus for the accidental localization of tubercle bacilli and the subsequent induction of a state of sensitization, presumably because of the prevalence therein of elements of the reticuloendothelial system. In the opinion of many foreign authorities, based on the experimental production of violent local ocular reactions by the injection of tuberculin into previously sensitized subjects, virtually every type of iritis, iridocyclitis and choroiditis is of conceivable tuberculous origin. These observers accept the reactions elicited as incontrovertible evidence of the tuberculous nature of the uveitis. As a matter of fact, Lagrange,<sup>4</sup> in his classic monograph on tuberculous iridocyclitis, asserted categorically that when biopsy is impracticable, the diagnosis of tuberculosis can be established definitely by means of the focal reaction to tuberculin alone. Moreover, he declared that tuberculous infection of the eye may manifest itself occasionally under the aspect of a common diffuse iritis, without specific lesions in the form either of nodules or of tuberculoma. Although certain other authors have described diffuse parenchymatous iritis as the initial stage of a disease which finally develops into the nodular, and thence into the tuberculomatous, variety, Lagrange<sup>4</sup> insisted that this iritis may never deviate from its ordinary inflammatory character.

Prominent among the opponents of the view set forth is Williamson-Noble,<sup>5</sup> who showed that tuberculous toxins apparently do not possess the absolute specificity attributed to them. Incidentally, through his tentative essays with the empiric application of tuberculin therapy in cases

1 Duke-Elder, W. S. *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1940, vol. 3, p. 2295.

2 Gullstrand, cited by Schneck, F. *Tuberkulose Infektion und Augenleiden*, Leipzig, Johann Ambrosius Barth, 1932.

3 Goldenburg, M. *Ophthalmic Tuberculosis*, in Goldberg, B. *Clinical Tuberculosis*, ed. 2, Philadelphia, F. A. Davis Company, 1939, vol. 1, p. 83.

4 Lagrange, H. *Etudes ophthalmologiques. La tuberculose de l'iris et du corps ciliaire*, Paris, Gaston Doin & Cie, 1933, vol. 4.

5 Williamson-Noble, F. A. *Brit J Ophth* **16** 285, 1932.



Fig 1—Growth through the base of the iris





of supposedly nontuberculous disease of the eye, this investigator obtained extraordinarily successful results, and so confirmed the observations of Wright<sup>6</sup> and others to the effect that tuberculin in the form of a bacillary emulsion represents an excellent antigen for employment against staphylococcal infections. In a contribution on the tubercle bacillus as a cause of obscure disease of the eye, published several years later, Williamson-Noble<sup>7</sup> cited the protocols of experiments conducted by Finnoff<sup>8</sup> which tended to cast doubt on the specific character of the tuberculin reaction in cases of spontaneous uveitis of suspectedly tuberculous origin (Moore<sup>8a</sup>).

Duke-Elder<sup>9</sup> expressed the belief that the disrepute incurred by the method of treatment of ocular tuberculosis with the various preparations of tuberculin should be ascribed in great part to the fatal consequences of the administration of moderately large doses with the object of eliciting successive focal reactions and of inducing thereby a local immunity. He stated that it is

essential to the meninges, rendered it possible to secure material for a detailed demonstration of the pathologic changes which occurred in the eye during the progress of the disease.

#### REPORT OF CASES

This first case represents an active form of secondary, malignant, uncompensated tuberculous uveitis, as described by Werdenberg,<sup>10</sup> with an exceedingly high degree of toxic sensitivity. With this form of ocular tuberculosis the use of tuberculin is positively contraindicated because of the unfavorable state of sensitivity, hence, conservative general and local treatment are required.

R. J., a man aged 20, a farmer, was first seen on Jan 13, 1941. At that time the right eye was inflamed and vision impaired. There was a slight palpebral discharge. Moderate injection of the ciliary processes was noted. Typical "mutton fat" deposits (keratic precipitates) were discerned on the posterior surface of the cornea. A dark orange-reddish mass appeared

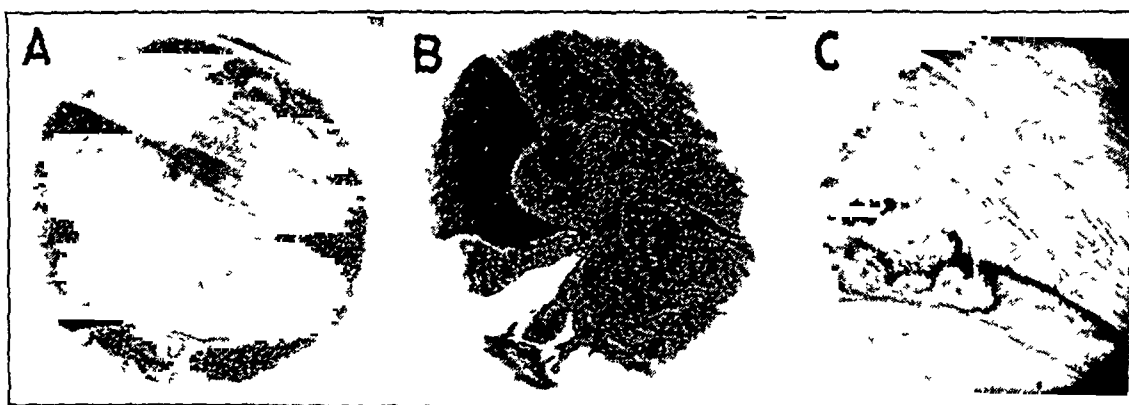


Fig 2—A, tubercle under Descemet's membrane, near the attachment of the pectinate ligament, B, conglomerate tubercle, extending into the anterior chamber, and C, scattered tubercles in the ciliary body and one tubercle on the internal surface of the sclera.

probable that optimal results are obtainable only if tuberculin is considered merely as a means for the production of a period of desensitization sufficiently protracted to inhibit allergic activity and thus to permit the establishment of an immune state. Hence, he concluded that tuberculin therapy should be regarded not as a curative expedient but as an adjuvant to the indispensable general treatment of uveal tuberculosis.

The following clinical observations have certain unusual features which characterize each of them. One relates to a malignant case of tuberculous iridocyclitis in which enucleation of the globe, performed to prevent extension of the proc-

to protrude through the base of the iris into the anterior chamber at 2 o'clock (fig 1). Numerous recently formed blood vessels were seen on the surface of this mass and on the body of the iris. The fundus was not visible. The intraocular tension was low. Visual acuity was 5/100 in the right eye and 2/26 in the left eye. With glasses, supplied by an optician, vision in the left eye was improved to 20/25.

Blood tests for typhoid and paratyphoid fever, brucellosis and tularemia, previously conducted by the family physician, had all given negative results, as had serologic tests, particularly the Wassermann and Kline tests. On the contrary, the Mantoux test gave a 2 plus reaction in seventy-two hours. Roentgenographic examination revealed two enlarged glands in the mediastinum. The lungs were normal.

The patient received three successive therapeutic applications of roentgen rays to the right eye, consisting of 375 r each, administered on January 18, January 25 and February 3 respectively, in conjunction with rest in bed and a diet rich in vitamin content. He was seen in consultation with Dr. Frank E. Burch on January 24. It was agreed that the patient had a

<sup>6</sup> Wright, A., cited by Williamson-Noble.<sup>5</sup>

<sup>7</sup> Williamson-Noble, F. A. *Brit. M. J.* 2:907, 1936.

<sup>8</sup> Finnoff, W. C., *Am. J. Ophth.* 7:81 (Feb.), 365 (May) 1924, cited by Williamson-Noble.<sup>7</sup>

<sup>8a</sup> Moore, R. F. *Tr. Ophth. Soc. U. Kingdom*, 55:3, 1935.

<sup>9</sup> Duke-Elder,<sup>1</sup> pp. 2315-2316.

<sup>10</sup> Werdenberg, E. *Klin. Monatsbl. f. Augenh.* 87:1, 1931.

conglomerate tubercle of the iris. Subsequent examination with the slit lamp showed a number of extensive lardaceous deposits on the posterior surface of the cornea. The aqueous flare was evident. The iris was bound down by posterior synechiae. A small, clearly defined tumor, heavily vascularized, was present on the temporal side. No decrease in the size of the mass occurred during the fortnight which followed the final application of the roentgen rays. Meanwhile the vision had diminished to mere perception of light. Accordingly, after a second consultation with Dr Burch on February 17, the affected eye was enucleated for fear that the process might extend to the meninges.

**Pathologic Report** (Dr Beulah Cushman)—**Macroscopic Examination.** The bulb measured 24 by 24.5 by 24.5 mm and was uniformly smooth (the optic nerve having been cut flush with the surface), but could not be transilluminated. The temporal segment measured 23 by 25 mm and the nasal segment 15 by 17 mm. The vitreous humor was soft, creamy and of fair consistency. In the nasal segment the ciliary body presented throughout its pars plana three distinct areas of thickening, the color ranging from a grayish to a creamy tint. The retina and the choroid were in place.

**Microscopic Examination.** **Cornea.** Edema, with round cell infiltrations, was present. Vascularization in the upper nasal quadrant extended forward into the stroma. The endothelium was swollen, and many large mononuclear cells and macrocytes, in part isolated and in part clumped, adhered to it. The anterior chamber contained fine granular matter, through which mononuclear cells and small lymphocytes were disseminated. Identically similar granular matter was noted in the posterior chamber. Nodules composed of epithelioid cells, surrounded by a thin covering of small lymphocytes, protruded into the anterior chamber from the pectinate ligament at the periphery and in one section (fig 2A) displaced the membrane of Descemet forward from the anterior surface of the ciliary body and the root of the iris. In another section a giant cell was observed to extend from the vicinity of the pectinate ligament. The recesses of the angle were partly occluded by cellular infiltration of the pectinate ligament, as well as the membranes along the anterior surface, and the swollen iris.

**Iris** (fig 2B). Edema and infiltration with plasma cells, small lymphocytes and disseminated Russell bodies were noted. A cellular membrane extended over the anterior surface and over clumps of cells composed of mononuclears, small lymphocytes and fibrin. The posterior layer of pigment was separated in certain areas and was adherent to the anterior capsule of the lens. Nodules consisting of small lymphocytes and epithelioid cells, which were present in the pigment layer, also adhered to the capsule. Here and there the layers of pigment were separated by the edema. In one section the iridic nodule was seen in the stroma immediately posterior to the sphincter on the left side, with nodules of small round cells adherent to the sphincter. Another section revealed a fine membrane which extended across the pupillary area and a nodule of epithelioid cells and lymphocytes which adhered to the capsule of the lens.

**Ciliary body and processes.** These structures were edematous, and large tuberculous nodules, consisting of small lymphocytes, epithelioid cells and an occasional giant cell, were present in the vascular portion of the ciliary body on the left side. In one section, six (fig 2C) nodules were counted in the ciliary body, one at the edge, pushing up the pigment epithelium,

and another adhering to the internal layer of the sclera (scleritis interna). Three smaller nodules, present in the unpigmented epithelium, produced dispersion and irregularity of the latter. A similar nodule was observed in one of the ciliary processes on the right side.

**Lens.** In most sections the lens appeared to have fallen out. The capsule was intact. Cellular deposits and a nodule, already described, adhered to the anterior capsule. In one section the posterior cortical fibers under the capsule on the right side were swollen. The posterior capsule of the lens and the condensation of the vitreous showed scattered large mononuclear cells.

**Vitreous.** The vitreous was converted into a delicate reticulum, containing scattered mononuclear cells derived from cellular precipitates over the flat portion of the ciliary body, and a nodule which apparently had broken into the vitreous.

**Choroid.** There was disseminated infiltration with small lymphocytes, and the pigment epithelium was separated from the rest of the choroid and was adherent to the retina.

**Retina.** In three sections, the retina was seen to be detached in the region of the macula, and also to be separated from the choroid, but entirely as an artefact, with the pigment epithelium adherent in many areas. The macular region was cystic, with spaces containing stained albuminous substance in the outer plexiform and nuclear layers. In one section a large cyst was observed in the fovea.

**Sclera.** Small lymphocytes had infiltrated the area of the limbus and the spaces around blood vessels. A large nodule, composed of lymphocytes and epithelioid cells, was encountered in the narrow space between the sclera and the ciliary body.

An anatomicopathologic diagnosis of tuberculous keratitis, iritis, cyclitis and scleritis interna (deep scleritis) was thereon established.

In this case, local treatment, rest in bed and a high vitamin diet were supplemented by roentgen irradiation. The tuberculous process failed to respond to treatment, and enucleation was advised and performed.

The following 3 cases illustrate tuberculous inflammation of the anterior segment. On entering a sanatorium, all the patients responded to treatment with rest in bed, a high caloric diet, abundantly supplied with vitamins, and tuberculin, administered in accordance with a carefully individualized plan of dosage. A second series of treatments, with tuberculin therapy distributed over a period of from one to two years, was advised for each of these patients as a safeguard against recurrence.

The 3 patients—H W, aged 35, J L, aged 12, and V K, aged 20—came to the office within a period of one year and a half. Each had had the condition described from six weeks to three months prior to consultation. All had pain, lacrimation, photophobia, blurring and diminution of vision. V K had a history of snow blindness, experienced in February 1941. Mantoux tests made on H W and J L gave positive reactions.

From April until October 1941, H W, who had a corneal ulcer on the right eye, was treated at the office. Silver nitrate was brushed on the eyelids, sulfanilamide powder was dusted into the cul-de-sac, and tincture of iodine was applied to the ulcer, which was also touched

with trichloroacetic acid. The local treatments afforded little relief. On Oct 10, 1941 the patient was admitted to the sanatorium. Roentgenographic examination of the chest failed to reveal tuberculosis but the Mantoux reaction was 3 plus. The patient was given a diet rich in vitamins and received old tuberculin in gradually enlarged doses twice a week until the initial dose of 0.001 mg had been increased to 1 mg. The corneal ulceration rapidly subsided, and the patient was soon relieved of his symptoms. The patient has experienced no recurrence of the ocular disease. Vision is now 20/25 in the right eye and 20/25 in the left eye.

J. L., when seen on May 4, 1940, had a corneal ulcer on the lower margin of the pupillary area of the right eye, with involvement of the stroma. Vessels extended to the margin of the ulcer, in the midthird of the stroma. The lesion was treated with mild cauterization and instillation of antiseptics into the eye. The depth of the ulcer increased progressively, until Descemet's membrane was exposed, with the possibility of herniation of the membrane. Dr. Archibald Olson placed a conjunctival flap over the area of the ulcer. The patient suffered from severe pain, and there was a terrific inflammatory reaction in the eye, with considerable haziness of the entire cornea and a purulent discharge from the eye. The sutures of the flap were cut, and sulfathiazole powder was insufflated in the eye every three hours. The discharge from the eye promptly decreased. The inflammatory reaction became less. By the end of ten days the ulcer had completely healed, with minimum corneal scarring.

Because of the presumed exposure to tuberculosis, a positive Mantoux reaction and the persistence of the ocular lesion on the right side, it was assumed that the ulcer was of tuberculous origin and, therefore, might be benefited by desensitization to tuberculin, hence, treatment in a sanatorium was advised. At the time of the patient's admission to the institution, a roentgenogram revealed a considerably enlarged hilus on the left side of the chest. Old tuberculin was administered twice a week, the dose commencing with 0.0001 mg, and injections of 1, 1.5, 2.2, 3.2, 4.7, 6 and 10 cc of a decreasing dilution were given until a dose of 0.1 mg was attained. Thereon the patient received 0.1 mg twice a week for fifteen weeks, without additional increase in the dose. She made a rapid recovery, and there has been no recurrence of her symptoms.

Examination of V. K. revealed an area of edema and increased thickening of all the layers of the cornea of the right eye. The sclera was injected. There was no vascularization of the cornea. Vision was 20/50 in the right eye and 20/20 in the left eye. At the sanatorium to which he was admitted, he was treated with rest in bed, and a 1 per cent solution of atropine sulfate was instilled into the right eye sufficiently often to keep the pupil widely dilated. A diet rich in vitamins was ordered, and subcutaneous injections of old tuberculin were administered at intervals of three days, the first dose being 0.001 mg. The lachrymation, photophobia and scleral injection rapidly subsided, with gradual diminution of the area of corneal opacity.

In the first 2 of these cases the condition was tuberculous keratitis of the relatively more frequent ulcerative type, and in the third case, mild tuberculous sclerokeratitis. A number of investigators have denied that the tubercle is a factor in the causation of inflammatory processes of the cornea and the sclera. However, in many

cases the diagnosis of tuberculous keratitis is based on the clinical aspect alone or on the therapeutic response to tuberculin. This situation is attributable primarily to the fact that corneal tissue affords an exceedingly poor medium for the culture of the bacillus and thus renders difficult the study of tuberculous lesions of the cornea. Histologic studies reveal no specific difference in appearance between sclerokeratitis and scleritis in general, certain of the phenomena present suggested that the condition was tuberculosis.

In a fifth case, one of tuberculous choroiditis, observations were made at occasional intervals for approximately ten years, during which the patient was submitted to a number of different forms of treatment, including tuberculin therapy. However, she received no systematic treatment with tuberculin until the disease had become well established. Despite this fact, the subsequent improvement in her general condition was distinct. Tuberculosis was assumed to be the cause of the retinal hemorrhage which occurred in this patient, whose somewhat unusual history follows. The antecedent optic neuritis probably was due, likewise, to infection with the tubercle bacillus, and not to the causes assigned in the past history. This tentative etiologic hypothesis was supported by the result of the physical examination of the patient's chest.

S. M. P., a woman aged 26, when first seen on June 18, 1917, presented a history of two previous attacks of optic neuritis in the left eye, one about two years earlier and the other within the preceding month. The first attack had been attributed to a nervous breakdown from overwork and the second to abscessed teeth. An examination on the aforementioned date revealed a hemorrhage (presumably associated with a metastatic embolus) involving the inferior temporal artery on the left optic disk.

While attended by Dr. Frank Burch, the patient had received six injections of old tuberculin during September and October of 1917, the dosage not being recorded. The report of a roentgenographic examination, on Oct 11, 1917, revealed tuberculosis of the glands of the thorax, with extension to the apex of the right lung. At that time lesions were discovered on the retina near the optic nerve and along the internal temporal vessels. On the same day the patient was admitted to a sanatorium for one month's observation and inoculation with a tuberculo-protein vaccine (von Ruck). She remained under treatment from Nov 21, 1917 to March 21, 1918. Beginning on Dec 27, 1917, she received a subcutaneous injection of 0.001 mg of old tuberculin. Tuberculin was administered in gradually increasing doses until Aug 17, 1918, when a maximal dose of 8 mg was attained.

After a lapse of nearly seven years, in the spring of 1925, the patient placed herself under the care of Dr. D. W. Wheeler, a tuberculographist. In a written communication to Dr. Wheeler, on March 14, 1925, Dr. Charles May, of New York, advised injections of tuberculin in minute doses every fourth or fifth day,

with gradual increase of the dose so as to avoid a reaction and continuation of the treatment from six months to one year. An initial dose of 1:40,000 dilution was recommended. Despite the fact that diagnostic tests with tuberculin had invariably given negative results when conducted on the patient, Dr May expressed his conviction that the hemorrhage which had been observed could be ascribed to tuberculous disease, hence the indication for the use of tuberculin. He added that even in the absence of a positive reaction to tuberculin, many ophthalmologists (including de Schweinitz) advocated the employment of injections of tuberculin.

Accordingly, an increasing series of treatments with old tuberculin, based on the foregoing scheme—0.10, 0.13, 0.15, 0.22, 0.25, 0.32, 0.47, 0.63 and 0.81 cc—was instituted by Dr Wheeler and continued from April 6 to July 26, 1925. Beginning on April 6, 1926, a second series of the same character was administered. The general condition of the patient was greatly improved by the systematic tuberculin therapy. The ocular lesion finally became quiescent. Meanwhile, the patient had lost the central vision of the affected left eye, owing to a lesion of the macula.

In January 1937 Dr Burch suggested the employment of nonspecific protein therapy in the form of injections with typhoid-paratyphoid vaccine. He expressed the belief that the consequent leukocytosis would prove extremely efficacious during the regressive stage succeeding the period of exudation, and that the resultant temporary impairment of vision would affect only slightly the already seriously diminished visual acuity of the left eye, while the incidental phagocytosis would be likely to benefit the ocular condition.

Perhaps the most significant features of the ocular disease in the case described here were the exceedingly protracted interval which elapsed between the onset of the optic neuritis and the loss of central vision of the left eye, particularly in the absence of a history of the occasional temporary obscurations of vision which generally precede total blindness resulting from arterial obstruction. The observation serves, also, to illustrate the fallacy of recourse to tuberculin therapy unless the latter is instituted promptly and is continued at regular intervals.

The following 7 cases exemplify the difficulty encountered in prevailing on patients with ocular tuberculosis to continue the treatment with tuberculin and to report the final results of such treatment. The patients, who were seen during the period from 1925 to 1941, ranged in age from 24 to 44 years. The records show that 5 of the women had a Mantoux reaction of 4 plus. The results of examination of the 7 patients were as follows:

**E A** The left eye revealed a small nodule on the iris, a posterior synechia and ciliary congestion, with scarring of the cornea. Vision was 20/20 in the right eye and 10/20 in the left eye.

**I S** The right eye was red and painful and presented ciliary congestion with keratic precipitates. Vision was 10/100 in the right eye and 20/25 in the left eye.

**R E C** The left eye presented a posterior synechia, congestion of the conjunctival vessels and a misty cornea. Vision was 20/20 in the right eye and was limited to light perception in the left eye.

**G A Y** Both eyes revealed opacities of the vitreous, deep corneal opacities and ciliary congestion. Vision was 10/100 in the right eye and 3/100 in the left eye.

**G M** The right eye had been inflamed for three weeks prior to consultation. The episcleral tissues appeared red.

**C T** The right eye presented tuberculous episcleritis. A nodule was discovered in the sclera above the pupil, at 12 o'clock. Vision was 6/100 in the right eye and 20/40 in the left eye.

**C S** The left eye revealed evidence of cyclitis. The fundus was normal. Vision was 20/25 in the left eye.

**R E C**, who was unable to come to the city to continue with tuberculin therapy, eventually lost the sight of the left eye. **C T** and **C S** did not return for treatments. **I S** received seven series of treatments with old tuberculin in six years. In 1934 vision with glasses was 20/65 in the right eye and 20/20 in the left eye. The right eye was quiescent. There was no pain. The general condition was much improved. **G A Y** received four series of injections of old tuberculin once a year for six years. In 1938 vision was improved to 20/50 in the right eye and to 20/65 in the left eye. Both eyes were quiescent, and there was no discomfort. She gained 15 pounds (6.8 Kg) in weight. To date, **G M** has received one series of tuberculin injections and is still under treatment, with complete subsidence of symptoms. Vision has improved to 20/25 in the right eye and 20/25 in the left eye.

The foregoing examples indicate that whenever tuberculin therapy was instituted and administered systematically for a sufficiently long period, the response was in general satisfactory. The result of the Mantoux test not only served to confirm the diagnosis but afforded an indication of the size of the initial dose of tuberculin to be employed.

Many patients cannot carry out a prolonged series of treatments. Distance to the physician's office prevented **R E C** from continuing her treatment. More and more people demand quick relief and will not consent to a two year program. Tuberculin should never be administered to a patient by even an internist unless he has special training in its use and has patience and perseverance. If the patient or the physician demands quick results, neither should consent to tuberculin therapy. Hurry means failure. Many physicians are afraid to administer tuberculin because, in their rush, they have given overdoses, with resulting reactions and disaster.

#### TREATMENT

It would be ideal if all patients with chronic uveitis of tuberculous origin could be admitted immediately to a sanatorium, but this is impos-

sible, for many reasons. In the sanatorium for tuberculous patients it is impossible for the patient to receive the necessary careful observation of his ocular lesion if he is under the care of the internist alone. The sanatoriums are already overcrowded and cannot possibly accommodate patients with ocular lesions. Economically, it does not seem necessary to hospitalize all patients with subacute or chronic uveitis. The purpose of the sanatorium is to offer special treatment for the patient with severe pulmonary disease and, secondarily, to isolate the patient. If the primary treatment in the hospital is rest in bed and a high vitamin and high caloric diet, the same results may be obtained by carefully supervised home treatment.

**Diet**—In the accompanying table a program for a high caloric diet is presented.

**Radium**—Many authors have had excellent results from the use of roentgen rays and radium in the treatment of ocular tuberculosis. For

**Roentgen Rays**—In treating any inflammatory condition of the eye it is essential to remember that, although the eye shows a relative tolerance for roentgen rays, damage may be done, especially to the conjunctiva and the more sensitive lens, unless care is taken. Fortunately, however, the dose of roentgen rays most efficient for the treatment of any inflammatory condition of the eye is well below the limits of tolerance of the conjunctiva and lens. Under such conditions there should be no danger of producing cataract in the adult.

In children the danger is greater because, as has been shown experimentally, the rapid growth of the lens during early life makes the structure much more sensitive and cataracts may be induced even with moderate doses.

In general, roentgen ray therapy for tuberculosis of the eye is moderately effective and is usually limited to rather small and repeated doses. By a small dose is meant from 10 to

*Average Values Obtained in Daily Food Analyses for Several Weeks*

Daily Average for Seven Day Periods	No of Calories	Carbo- hydrates, Gm	Protein, Gm	Fat, Gm	Calcium, Gm	Phos- phorus, Gm	Iron, Gm	Vitamins, International Units			
								A	B <sub>1</sub>	C	B <sub>2</sub>
	2,646	256	86	132	1.1368	1.72	0.01238	6,539	423	1,593	735
	2,617	263	82	135	1.3700	1.77	0.01331	6,510	421	1,312	681
	2,867	303	90	118	1.3550	1.72	0.01107	9,506	540	1,614	628
	3,005	324	89.5	150	1.3912	1.71	0.01501	5,707	424	1,689	692
	3,033	341	84.5	168	1.3789	1.60	0.01556	6,605	437	1,506	648
	3,041	356	90	168	1.3900	1.71	0.01458	8,119	101	1,718	782
Daily average for week of November 16-22	2,965	303	92	156	1.6021	1.87	0.01986	8,735	161	1,678	739
Average person's requirement			70		0.68	1.3	0.012	5,000	300	600	600

many lesions of the anterior segment of the eye, especially the cornea, treatment with radium is often satisfactory.

In the treatment of inflammatory lesions of the eye, comparable results may be obtained with small doses of radium. However, it is more difficult to obtain a uniform distribution with radium than with roentgen rays.

For lesions involving the cornea, the beta rays of radium may be used. If possible, the portion of the cornea not involved should be protected by a properly constructed lead shield, and the radium elements used in 0.5 mm point steel needles. The dose is 100 to 150 milligram minutes, and three to four treatments are given at weekly intervals.

For the more deep-seated lesions, the gamma rays are utilized. The radium element may be used in 0.5 mm point needles, held in place by a wax mold. A single dose of 25 to 50 milligram hours at a distance of 2.5 cm may be sufficient for the acute inflammatory conditions. Lesions of a chronic nature require three or four weekly treatments.

30 or 40 per cent of the erythema, or tolerance, dose for the skin of a young person. In terms of the international quantitative unit of roentgen radiation, this would mean from 40 to 160 r (measured in air).

The treatment is given directly over the eye, with the following factors: 100 to 120 kilovolts, 5 milliamperes, a 1 mm aluminum filter, a distance of 30 cm and 3 by 4 cm or 6 by 8 cm fields. For an adult, the dose depending on the precise character of the lesion, from 75 to 100 r is given once a week over each eye for four weeks. This series may be repeated, if necessary, in two months.

For chronic inflammatory lesions of the eye, the dose should be larger than for acute conditions, but it should never be so large as to endanger the structures of the most sensitive ocular parts, namely, the conjunctiva and the crystalline lens.

**Gold Sodium Thiosulfate**—Gold salts have been used as nonspecific treatment for ocular tuberculosis. The patient may become sensitive to the drug and present symptoms of diarrhea,

cutaneous rash and edema. Gold salts have fallen into disrepute with practitioners because of manifestations of intoxication and intolerance which occurred in consequence of incorrect treatment.

Gold sodium thiosulfate is administered twice a week for at least fifty or sixty injections. The dose is usually 25 mg. Some physicians start with an initial dose of 10 mg, each dose being increased by 5 mg, to a maximum of 50 mg.

**Typhoid H Antigen**—Typhoid H antigen was advocated by Brown<sup>11</sup> for the treatment of intraocular inflammation in cases in which non-specific immunization is an accepted therapeutic measure. A dose of 0.06 cc of a solution of typhoid H antigen is administered intradermally. If there is no local reaction in thirty minutes, the patient is not sensitive to the antigen. Then 5,000,000 to 10,000,000 units of typhoid H antigen is given intravenously. In twenty-four hours another 5,000,000 units is given intravenously. Twenty-four hours after the last injection the paracentesis is performed.

#### MANTOUX DIAGNOSTIC TESTS

**Purified Protein Derivative of Tuberculin**—Seibert's purified protein derivative is recommended for the intradermal test of tuberculosis because it is uniform in strength. This preparation is expensive. It deteriorates quickly and cannot be used for more than three days after preparation.

The test is carried out with doses of two strengths. Persons who do not react to an injection of the first test strength have a second injection forty-eight hours later with a dose of the second test strength.

**First Test Strength**—An intradermal injection of 0.1 cc from a vial containing 0.0002 mg of purified protein derivative is made on the forearm. Readings are made in forty-eight hours.

**Second Test Strength**—If no reaction occurs in the first test, an intradermal injection is made on the forearm of 0.1 cc from the vial containing 0.05 mg of purified protein derivative, a dose which is two hundred and fifty times that in the first test.

If a quantitative determination is desired, according to Adler, an initial dose of 0.000001 mg per cubic centimeter of purified protein derivative of the first test strength may be given intradermally. The dose is increased tenfold

for each succeeding intradermal injection until a positive reaction is obtained. This is the quantitative test of Aronson.

**Old Tuberculin**—The old tuberculin of Koch is used intradermally for the diagnosis of tuberculosis. This is the Mantoux test. Old tuberculin will not deteriorate as rapidly as purified protein derivative. It is much less expensive.

Three dilutions of old tuberculin are made, as follows: 1 100,000, 1 10,000, and 1 100. An intracutaneous injection of 0.1 cc of solution 1 100,000 of old tuberculin (0.001 mg) is given. If no local reaction follows, 0.1 cc (0.01 mg) of solution 1 10,000 of old tuberculin is administered intracutaneously. Later, 0.1 cc (0.01 mg) of solution 1 100 of old tuberculin is injected intracutaneously. If no local reaction is obtained with the usual test of three dilutions, the strength may be increased, 1, 5 or, finally, 10 mg of old tuberculin being injected intracutaneously.

The cutaneous reactions have been classified as follows:

Grade	Area of Redness and Edema, Diameter in Mm
+	5—10
++	10—20
+++	More than 20
++++	Pronounced, some necrosis

Haessler<sup>12</sup> stated:

If one does not believe in the efficiency of specific therapy with tuberculin, there is hardly a logical reason for differentiating tuberculosis from the many other etiological factors which cause inflammation in the eye.

#### PREPARATION AND ADMINISTRATION OF OLD TUBERCULIN

In preparing the solutions of old tuberculin, phenol, in 0.25 per cent concentration in isotonic solution of sodium chloride, is used as a diluent. The solutions are stable for about two weeks if kept in an ice box.

To make a series of dilutions, 1 10, 1 100, 1 1,000, and so on, the bottles are numbered to correspond to the number of zeros in the denominator: for example, solution 1/1, 2/1, 3/1, and so on.

The data for the series of dilutions may be summarized as follows:

Old Tuberculin, Cc of Solution No	Diluent, Cc	Dilution	Solution No	Amount of Old Tuberculin, Mg per Cc of Solution
0.1 cc	0.9	1 10	1/1	100.0
1.0 cc of 1/1	9.0	1 100	2/1	10.0
1.0 cc of 2/1	9.0	1 1,000	3/1	1.0
1.0 cc of 3/1	9.0	1 10,000	4/1	0.1
1.0 cc of 4/1	9.0	1 100,000	5/1	0.01
1.0 cc of 5/1	9.0	1 1,000,000	6/1	0.001

<sup>11</sup> Brown, A. L. Use of Typhoid H Antigen Before Intracocular Operations, Arch Ophth 19 181 (Feb) 1938

<sup>12</sup> Haessler, F. H. Minnesota Med 26 161, 1943

The following scheme, computed by Pope, and employed at the Trudeau Sanatorium, is based on a logarithmic scale and is arranged so that when the dose is increased from 0.1 to 1 cc. of any solution, two to twelve doses may be employed, while the rate of increase of the dose in each case is always constant

*Doses (Logarithmic Scale)*

1	2	3	4	5	6	7	8	9	10	11	12
1	1	1	1	1	1	1	1	1	1	1	1
	32	22	18	16	15	14	13	13	13	12	12
	10	47	32	25	22	20	18	17	16	15	15
		10	56	40	32	27	24	22	20	18	18
			10	63	47	37	32	28	25	23	22
				10	68	52	42	36	32	29	26
					10	72	56	47	40	35	32
						10	75	60	50	43	38
							10	77	61	53	47
								10	80	66	56
									10	80	68
										10	8
											10

Several rates of increase for the use of tuberculin were employed. After the maximum dose with solution 6/1 was given, the series of injections were repeated with solution 5/1. The treatment is continued through the series of dilutions until a dose of 1 mg. is reached. Ordinarily, the dose is not carried above 1 mg. of old tuberculin. To avoid all local and gen-

eral reactions, the patient takes and records his temperature three times a day, after each injection of old tuberculin, for thirty-six hours. If signs or symptoms of reaction occur, one or two treatments are omitted and the dose is reduced when the injections are started again.

In the treatment of patients with ocular tuberculosis the aim is to cure the entire process in the organism by general treatment and not by treatment only of the local disease. Its basis is a knowledge of the entire disease picture, of the principal clinical forms of ocular tuberculosis, of the primary, generally intrathoracic origin of the infection, and of generalized tuberculosis.

The point of attack of any useful therapy is the organism as a whole, especially in the initial phase of the disease, and the attempt should be made to change the key, to swing or transpose the constitutional tuberculosis into a more benign form of the disease. A second favorable phase is that in which there is a favorable response to aggressive general kind of local treatment, such as specific therapy, treatment with x-rays and so forth. Two main clinical groups of ocular tuberculosis stand in therapeutic opposition: malignant, exudative forms with the subjects toxin-sensitive, calling for conservative, general and local treatment, on the one hand, and on the other, benign, productive or fibrous forms, with the subjects less toxin-sensitive, indicating a more aggressive therapy.<sup>13</sup>

812 Medical Arts Building

<sup>13</sup> Werdenberg. Useful and Harmful Therapeutics in Tuberculosis, *Arch. Ophth.* **13** 303 (Feb.) 1935.



# COMPARISON OF THE OBLIQUE EXTRAOCULAR MUSCLES

WILLIAM E KREWSON III, M D

PHILADELPHIA

The oblique muscles in many respects are the most interesting of all the extraocular muscles. They have been regarded by most authors as a pair, and emphasis is usually placed on their similarity to each other and to the rectus muscles. When the superior and the inferior oblique muscles are considered separately, however, and are compared one with the other, many significant contrasts are revealed. In presenting such a comparison, therefore, this paper expresses only in a rather unique form that of which most ophthalmologists are already cognizant.

## ANATOMIC RELATIONS

Embryologically, the orbital muscles are said to be derived from the head, or cephalic, mesoblastic somites. The inferior oblique muscle, like all the muscles supplied by the third nerve, is derived from the first somite, while the superior oblique muscle originates from the second somite.

The superior oblique muscle arises in the posterior part of the orbit from the mesial aspect of the annulus of Zinn and is contiguous with the origin of the internal rectus muscle. The belly of the muscle extends anteriorly, close to the nasal wall, to the upper, inner and posterior surface of the orbital rim, where it is reflected around the trochlea. This "pulley" is a ligamentous, looplike attachment in the fovea trochlearis of the orbital surface of the frontal bone. From the trochlea to its insertion on the globe, the superior oblique muscle is entirely tendinous, about 20 mm in length, according to Whitnall.<sup>1</sup> It is the longest muscle and has the longest tendon of all the extraocular muscles.

The inferior oblique muscle, by way of contrast, is the shortest of the extraocular muscles and is composed purely of striated muscle fibers, having practically no tendon at all. The only muscle arising in the anterior part of the orbit it has for its origin a small fossa in the maxillary bone just inside the lower inner quadrant of the orbital rim. It proceeds posteriorly and laterally and is inferior to the globe.

The oblique muscles are ensheathed, like the rectus muscles, between the internal capsule of

Tenon's fascia, on their ocular surfaces, and the external capsule, on their orbital surfaces. According to Motais (cited by Maddox<sup>2</sup>), the internal superior check ligament of the superior rectus muscle applies itself to the tendon sheath of the superior oblique muscle. The check ligament of the inferior oblique muscle, on the other hand, leaves the muscle sheath 8 to 10 mm from the origin of the muscle and crosses obliquely forward and outward to the outer angle of the orbit. Being purely a fibrous aponeurosis, it not only acts as a check to the relaxation or extension of the muscle but modifies the effect of the muscle pull during contraction, as will be seen later. By way of contrast, then, the superior oblique muscle may be said to have no real check ligament of its own, while the inferior oblique muscle has the longest and strongest in the orbit.

Howe,<sup>3</sup> in a large series of dissections and plottings, presented a comparison of the insertions of the two muscles. The insertion of the superior oblique muscle is variable, its tendon spreads out across the vertical meridian in a backwardly directed convex line. According to Fuchs,<sup>4</sup> in emmetropic eyes the average insertion is 10.7 mm in breadth. The anterior end is about 14.6 mm from the optic nerve and lies in the same meridian as the lateral border of the superior rectus muscle, while the posterior end is about 7.5 mm from the nerve. Again, by way of contrast, the insertion of the inferior oblique muscle is rather constant in its location (so much so that it may be used in operations for retinal detachment as one of the few definite landmarks on the posterior surface of the globe). Having no real tendon, the muscle fibers are inserted directly into the sclera on the horizontal meridian of the globe, making a right angle with the external rectus muscle. The line of insertion is about 10 mm long, and in normal eyes its center is 2.2 mm from the spot cor-

2 Maddox, E. E. *Tests and Studies of the Ocular Muscles*, Philadelphia, Keystone Publishing Co., 1907.

3 Howe, L. *The Muscles of the Eye*, New York, G. P. Putnam's Sons, 1908, vol. 1.

4 Fuchs, E. *Text-Book of Ophthalmology*, translated by A. Duane, ed. 7, Philadelphia, J. B. Lippincott Company, 1923.

1 Whitnall, E. S. *The Anatomy of the Human Orbit*, ed. 2, London, Humphrey Milford, 1932.

responding to the fovea and 5.2 mm from the optic nerve. An obvious contrast, which is not generally realized, is the fact that the insertion of the superior oblique muscle is anterior to the superior pair of vortex veins, while the inferior oblique muscle is inserted posterior (and lateral) to the inferior pair of vortex veins.

Little of the superior oblique muscle is taken up in the so-called arc of contact, while nearly half the length of the inferior oblique muscle is wrapped around the globe. Both oblique muscles pass beneath the corresponding vertically acting rectus muscles, and this undoubtedly acts to their mechanical disadvantage in certain ocular movements, as noted later.

With regard to the nerve supply, a difference is again seen between the oblique muscles. The superior oblique muscle is innervated by the trochlear nerve, which arises from the nucleus of the fourth nerve on the contralateral side of the medulla. The inferior oblique muscle is supplied by a branch of the oculomotor nerve, which originates in a collection of centers composing the nucleus of the third nerve. Maddox,<sup>2</sup> in 1907, stated that it is probable that the nucleus of the fibers to the inferior oblique muscle lies on the opposite side of the median plane, so that a decussation of the fibers of the third nerve analogous to that of the trochlear nerve is necessary, but this has not been substantiated. Some authors have indicated that the fibers to the inferior oblique muscle arise from the ipsilateral nucleus, but Bing<sup>5</sup> and Whitnall<sup>1</sup> expressed agreement that there is probably some degree of bilateral innervation.

#### ACTION OF THE OBLIQUE MUSCLES

The planes of action of the two oblique muscles were said by Maddox<sup>2</sup> to be identical, each making an angle of 51 degrees with the median plane. From the corrected figures of Volkmann,<sup>6</sup> however, the tendon of the superior oblique muscle makes an angle with the median plane of 55°21', while the inferior oblique muscle makes an angle of only 50°57'. This means that the inferior oblique muscle has a greater vertical purchase on the globe than does the superior oblique muscle, i.e., its plane of action is closer to the anteroposterior diameter. In fact, the inferior oblique is actually pulled more closely toward parallelism with the median plane by its check ligament, which pulls the muscle belly

laterally, as previously noted. Thus the inferior oblique muscle contributes more of its energy to elevation than the superior oblique contributes to depression, the ratio being 60/57, or 42 per cent to 37 per cent, as indicated by Verrill.<sup>7</sup>

Maddox<sup>2</sup> pointed out that the speed with which a muscle's point of insertion moves is proportional to its length. The fact that the inferior oblique muscle is longer than the "effective" portion of the superior oblique muscle and that its insertion is farther from the center of rotation means that for the same amount of contraction the inferior oblique muscle will produce a greater vertical displacement of the eye than will the superior oblique muscle.

Duane<sup>8</sup> implied that when the eye is in the primary position the vertical pull of each of the oblique muscles is about equal to that of the opposing vertically acting rectus muscle. However, Weiland,<sup>9</sup> Maddox<sup>2</sup> and Tschermak<sup>10</sup> agreed that in such a comparison the oblique muscles exhibit much less vertical pull than their antagonists.

As is quite evident, the vertical pull of the oblique muscles increases as the eye is internally rotated and the anteroposterior diameter of the globe more nearly approaches the planes of action of the respective muscles, being maximum for the inferior oblique muscle at 50°57' and for the superior oblique muscle at 55°21' of internal rotation. The elevating or depressing action, as the case may be, decreases as the eye is externally rotated.

In like manner, because the insertions of the oblique muscles are lateral to the anteroposterior diameter of the globe, each produces a torsional effect. On contraction the superior oblique muscle causes intorsion, the inferior oblique muscle, being wrapped around the lower portion of the eye, causes extorsion. The torsional effects of the two oblique muscles although opposite in direction, are about equal in amount. The maximum torsional effect of the oblique muscles, in contradistinction to their maximum vertical pull, as just mentioned, is obtained when the eye is externally rotated and the anteroposterior diameter of the eye approaches a posi-

7 Verrill, C. D. *Movements of the Eyes*, in Beiers, C. *Eye and Its Diseases*, Philadelphia, W. B. Saunders Company, 1936, chap. 50.

8 Duane, A. *A New Classification of the Motor Anomalies of the Eye*, New York, J. H. Vail & Co., 1897.

9 Weiland, C. *The Law of Listing and Some Disputed Points About Its Proof*, *Arch. Ophth.* **28**, 191, 1899.

10 Tschermak, A. *Augenbewegungen*, in Bethe, A., von Bergmann, G., Emden, G., and Ellenger, A. *Handbuch der normalen und pathologischen Physiologie*, Berlin, Julius Springer, 1931, vol. 12, pt. 2.

5 Bing, R. *Compendium of Regional Diagnosis in Lesions of the Brain and Spinal Cord*, ed. 11, St. Louis, C. V. Mosby Company, 1940.

6 Volkmann, A. W. *Zur Mechanik der Augenmuskeln*, *Ber. u. d. Verhandl. d. k. Sachs. Gesellsch. d. Wissensch.* **21**, 28, 1869.

tion of a right angle to the plane of action of the muscles. The torsional action is diminished with internal rotation and is nil when the line of fixation coincides with the respective muscle planes.

The effect of the oblique muscles around the vertical axis of rotation remains to be considered. The oblique muscles tend to rotate the eye externally, and, just as for torsion, this tendency increases as the eye continues to rotate outward and diminishes with internal rotation. Certainly, this is true in the case of the superior oblique muscle, the insertion of which on the upper, outer and posterior surface of the globe necessitates the tendon's passing posterior to the vertical axis. On contraction of the superior oblique muscle, its origin (and the posterior pole of the eye) is drawn toward the midline, i.e. the eye is rotated outward.

The same horizontal action in the form of external rotation is ascribed to the inferior oblique muscle. This teaching is in accordance with accepted clinical observations and has been endorsed by Duane,<sup>11</sup> Peter,<sup>12</sup> Maddox,<sup>2</sup> Savage,<sup>13</sup> Stevens<sup>14</sup> and others. It is based on the assumption that the inferior oblique muscle passes posterior to the vertical axis of rotation, as does the superior oblique muscle. Reference to Volkman's<sup>6</sup> anatomic measurements, however, shows that the plane of the inferior oblique muscle actually passes anterior to the vertical axis. If this is true, in contraction the muscle must pull its insertion (and posterior pole) away from the midline, or internally rotate the eye. Furthermore, as internal rotation continues, the insertion and line of pull of the muscle both become increasingly more anterior to the center of rotation, and inward rotation is accentuated. This is quite the opposite of the superior oblique muscle, the lateral rotational effect of which, as already noted, diminishes as the eye is turned inward. During external rotation, on the other hand, the plane of the inferior oblique muscle will reach a point where it passes through the vertical axis, at which time the horizontal pull will be nil, then, as the eye continues to turn outward the pull of the muscle will pass posterior to the vertical axis, and beyond this point, as with the superior oblique muscle, it will increase in its external rotating component.

It seems strange that after almost a century the true action of the inferior oblique muscle

should still be in apparent doubt. The orthodox belief that the muscle acts as an external rotator is supported by many eminent clinical observers, while the position of the other school, which maintains the action to be that of an internal rotator, is based on accurate anatomic dissection and sound mathematical computation. When one recalls that in ordinary use emmetropic persons do not move their eyes more than 12 degrees to the right or left before movements of the head become a factor, as Fischer<sup>15</sup> has shown, the true action of the inferior oblique muscle from the position of "eyes front" becomes of increased importance.

#### PARALYSIS

Paralysis is probably the most common pathologic condition affecting the individual extraocular muscles, and here, again, a contrast is found between the two oblique muscles. The superior oblique muscle is the second most frequently paralyzed of all the extraocular muscles (being exceeded only by the external rectus muscle), while the inferior oblique muscle certainly presents the lowest incidence of isolated oculomotor paralyses. The inferior oblique muscle derives its innervation from the same branch of the third nerve as do the ciliary muscle and the sphincter muscle of the iris, hence, in cases of postorbital lesions paralysis of the inferior oblique muscle is accompanied by internal ophthalmoplegia.

Paralyses of both the superior and the inferior oblique muscle, as Peter<sup>12</sup> indicated, present the usual symptoms, among which the most diagnostic are ocular deviation, limitation of movement, false projection and diplopia. Although "the eye turns away from the field of action of the paralyzed muscle," Peter<sup>12</sup> emphasized the fact that the deviation may not be very noticeable since the oblique muscles act vertically and there is more than one elevator and one depressor for each eye. However, paralysis of the inferior oblique muscle, for anatomic reasons already noted, should produce a greater ocular deviation than a corresponding paralysis of the superior oblique muscle. Limitation of movement and vertical diplopia will be greatest when the eye is turned so that the anteroposterior diameter of the globe is in the plane of action of the muscle, i.e. where the muscle has its maximum vertical component. With paralysis of the superior oblique muscle as has been noted, this maximum is reached when an attempt

11 Duane, A. The Monocular Movements. *Arch Ophth* 8:530 (Oct.) 1932.

12 Peter, L. C. The Extra-Ocular Muscles, ed. 3, Philadelphia, Lea & Febiger, 1941.

13 Savage, G. C. Ophthalmic Myology, Nashville, Tenn., privately printed, 1902.

14 Stevens, G. T. The Motor Apparatus of the Eye, Philadelphia, F. A. Davis & Co., 1906.

15 Fischer, F. P. Ueber die Verwendung von Kopfbewegungen beim Umhersehen, *Arch f. Ophth* 113:394 1929.

is made to turn the eye down and in, with paralysis of the inferior oblique muscle, when an attempt is made to turn the eye up and in.

Mauthner (cited by Maddox<sup>2</sup>) showed that the separation of the images of the two eyes is greater with paralysis of the inferior oblique than with paralysis of the superior oblique muscle, since the former muscle as previously mentioned has a greater "arc of contact," is inserted farther from the center and pulls nearer the midline, a position which gives it a greater vertical purchase on the globe. With paralysis of the superior oblique muscle, which acts as an intorter, the false image leans to the normal (opposite) side; with paralysis of the inferior oblique muscle which acts as an extorter, its false image leans to the affected (same) side. Paralysis of both oblique muscles produces a slight homonymous lateral separation of the images (except in cases of preexisting exophoria), a phenomenon which confirms the contention of Maddox<sup>2</sup> and verifies the results of Volkmann's<sup>6</sup> studies, namely, that the oblique muscles do not rotate about a common axis.

#### SUMMARY

The oblique extraocular muscles present many interesting contrasts. The superior oblique muscle arises at the optic foramen and is the longest muscle in the orbit, the inferior oblique muscle arises at the orbital foramen and is the shortest. The superior oblique muscle has the longest tendon of all the extraocular muscles but no check ligament, while the inferior oblique muscle has no tendon but has the longest check ligament. The superior oblique muscle has the most variable of insertions, the line being usually on the vertical meridian, anterior to the vortex

veins, the inferior oblique muscle has the most constant of insertions, being located on the horizontal meridian and posterior to the vortex veins. The arc of contact for the superior oblique muscle is shorter than that for any of the other muscles, that for the inferior oblique muscle is the longest of all. The superior oblique muscle has a contralateral innervation, and the inferior oblique muscle, an ipsilateral or a bilateral representation. The superior oblique muscle acts as a depressor, and the inferior oblique as an elevator, their respective actions increase as the eye turns inward and decrease as the eye turns outward. The former acts as an intorter and the latter, as an extorter, both torsional actions increase as the eye is turned outward and decrease as it is turned inward. Both muscles are reputed to act as external rotators, which action increases as the eye turns outward and decreases as the eye turns inward. In the case of the inferior oblique muscle, however, there may still be a question whether it acts as an internal or as an external rotator. The superior oblique muscle is the second most frequently paralyzed muscle, the inferior oblique muscle is the least frequently involved, and then is often accompanied by internal ophthalmoplegia. With paralysis of the superior oblique muscle limitation of movement and vertical diplopia are greatest when the eye is turned down and in, and with paralysis of the inferior oblique muscle, when the eye is turned up and in. Vertical diplopia is greater with paralysis of the inferior oblique muscle than with paralysis of the superior oblique muscle. The false image representing the superior oblique muscle leans to the normal (opposite) side, and that of the inferior oblique muscle leans to the affected (same) side.

1930 Chestnut Street

# PROSTHESES FOR THE EYE AND ORBIT

ADOLPH M BROWN, M D

CHICAGO

After destruction of the eye, a glass eye is sufficient prosthesis unless the eyelids are also missing. Patients who require only a glass eye do not present themselves at the prosthetic laboratory. Most commonly a prosthesis is required after surgical exenteration of the entire orbital contents. The patient is confronted with a number of choices: (a) to flaunt the defect, walking about with it visible and making no effort to conceal it, (b) to hide the defect with a bandage, and (c) to substitute a prosthesis for the lost organ or portion of an organ.

A prosthesis for the orbit should not be made until the skin of the area is adequately healed, unless provision is made on the under surface of the prosthesis for protection of any raw or granulating areas. Figure 1 shows a 20 year old woman who had had exenteration of the entire orbital contents for glioma six years previously. The orbital wound opened at the region of the inner canthus into the sphenoid sinus. The sinus had been draining through this opening for years. The prosthesis illustrated was designed so that there was no contact of rubber and skin near the open area. When the patient wore her prosthesis, there was less crusting and she apparently enjoyed more comfort.

The skin of the upper part of the cheek, around the outer canthus of the eye, is supported on unusually delicate beds of fat. For this reason, a prosthesis planned and processed in the ordinary way makes the eyes appear asymmetric. After several disappointments in cases in which additional corrections were required, I realized that the impressions had been made while the patient was supine. The prosthesis had been designed on these impressions, and when they had been fitted the patient was again supine. When the patient was upright the prosthetic eye seemed lower than the normal eye, although it had been placed correctly by calibration. The weight of even a light prosthesis was sufficient to cause the orbital edge of the skin to sag  $\frac{1}{8}$  to  $\frac{1}{4}$  inch (0.3 to 0.7 cm) below its normal position.

Two overcorrections are necessary, therefore, in making a prosthetic eye and lids. In the first place, the entire orbit should be sculptured slightly higher on the face than its opposite. In the second place, the conjunctiva should be slightly more visible in the prosthesis than in the normal eye. In other words, the artificial eye must be slightly more opened than the normal eye.

In making a prosthetic eye and lid an impression is made of the normal eye first. This impression may be made as usual with plaster, with the eye closed, or it may be made with a gelatinous compound, with the eye open. While the positive mold is being cast, the patient is sent to have the normal eye matched for a glass eye. If possible, it is advisable for the patient to obtain two glass eyes. Glass eyes are almost invariably too large in circumference, because they are made to be tucked into living eyelids. When the prosthetist receives the glass eye, he mounts it in molding clay in its correct anatomic position and determines how much trimming of the edge of the glass eye will be necessary. The border of excessive artificial conjunctiva is marked with a wax pencil, and the excess glass is ground away. The glass of an artificial eye is carefully tempered, but it is still fragile, and breakage during the grinding is not uncommon. Once the edge is trimmed, the artificial eye is ready to be mounted accurately in the molding clay. By careful mensuration of the model and the patient, the site for the eye is determined, and the sculpture proceeds with the glass eye in place. The site for the eye is corrected slightly, so as to place it a little above its true position on the face. The upper lid of the sculptured model is made slightly thicker than the lid of the opposite side, to provide enough thickness for a trench to be cut. This fissure will contain the "roots" of the artificial eyelashes to be added later. When the eye and orbit are accurately sculptured, the model is ready for the casting of the second half of the mold. It is not necessary to draw in the fine pores and epithelial tracery that other prostheses require. After the top half of the mold has set, the parts are separated, the modeling clay is washed out, and the glass eye is

From the Eye and Ear Infirmary, the University of Illinois

retrieved. Later, when the mold is ready to cast in rubber, the glass eye will be lightly glued in place on the upper half, so that after the rubber is poured it will be accurately embedded in the rubber lids.

In making a prosthesis for exenteration of the orbit only, a negative impression is made with No. 1 molding plaster, and from this a positive impression is cast in dental stone or hydrocol. The eye is then sculptured on the positive cast. To sculpture the eye, the prosthetist must rely on his patient to sit for him, so that he may make the prosthetic eye a mirror image of the remaining one. This is sometimes difficult for both the patient and the doctor. In such cases it is advisable to make an impression of the

within the critical period, and the margin for error was rather narrow.

Modern compounds for negative impressions are greatly improved. They are supplied in the form of molding powders and require mixing with distilled water only. They are then spatulated to a smooth, air-free mixture, and the casting of the impression is done in the usual manner. Gelatinous impression compounds are placed on the eye at a relatively low temperature. There is no discomfort to the patient, no irritation and no subsequent chemosis, and particles rarely remain in the eye after the cast has been removed. Gelatinous impression compounds are easy to handle. They require no special equipment and produce accurate, detailed impressions

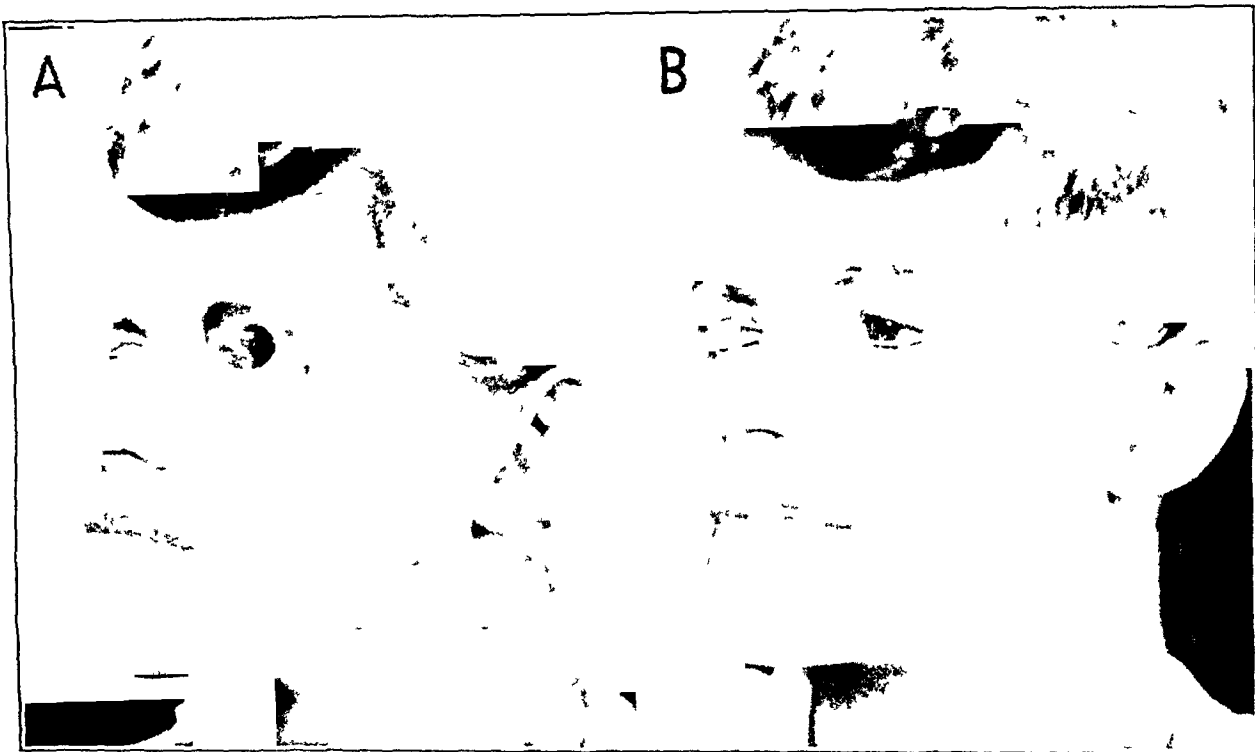


Fig 1—Face after surgical exenteration of the entire orbital contents for retinoblastoma (A) without and (B) with a prosthesis. The prosthesis had to be designed as a relatively thin sculptured patch to avoid contact with the exposed sinuses.

remaining eye while it is open for reference while sculpturing the prosthesis.

Negocoll was formerly used for making impressions with the eye open. In order to make an impression of this type it is necessary, of course, to anesthetize the conjunctiva. When Negocoll was used, it was necessary to stir the hot mixture and cool it slowly until the proper temperature was reached so that a satisfactory negative impression could be made and, at the same time, the conjunctiva and eyelid would not be injured by the heat. Other gelatin compounds also required boiling and stirring and then had to be cooled slowly to about 106 F (40 C), at which temperature they made effective impressions and caused no harm to the eye. But these compounds had to be used quickly and delicately

of eyes and even of overhanging wrinkles containing undercuts. In handling them, flexible rubber bowls may even be dispensed with, if necessary, and paper cups substituted. Ordinarily, however, a rubber bowl for mixing is required, together with spatula and a graduate. When mixed with distilled water, these compounds react chemically to form a highly elastic gelatinous mass. After a few attempts the operator can best determine the amount of powder and distilled water suitable for his particular needs.

The following method has proved satisfactory in my work, but it can be variously modified to meet individual requirements. The eye is anesthetized before the impression is made. Ordinarily 2 drops of anesthetic is placed in the eye

about five minutes before the powder is mixed. A few minutes should be allowed to elapse between instillations. Another drop may be instilled when the operator begins the spatulation. A minute or two later a fourth drop of anesthetic may be instilled, with a drop of epinephrine hydrochloride solution if desired. Pour the required amount of distilled water into a rubber bowl. Tap the container of molding compound on the table to settle the contents, then add 1 Gm of powder for every 5.5 cc of water. Roughly, bulk for bulk of powder and water can be mixed together. The graduate should be thoroughly dry before the powder is measured. Mix the water and powder, and spatulate the mixture till it is smooth. The bowl may now be tapped on the table a few times to

moved in the usual manner and is ready for fixing.

The setting time of gelatinous molding powders may be hastened (1) by using warmer water, (2) by spatulating more vigorously and for a longer time and (3) by reducing the proportion of water used. It is sometimes necessary to achieve a longer setting period, so that alterations can be made in the negative impression while it is still moldable. The setting time can be lengthened (1) by using cold water or ice water, (2) by slower, more gentle spatulation and (3) by increasing the proportion of water used.

Fixatives for gelatinous molding compounds are generally supplied in the form of tablets that are dissolved in water to make a solution which

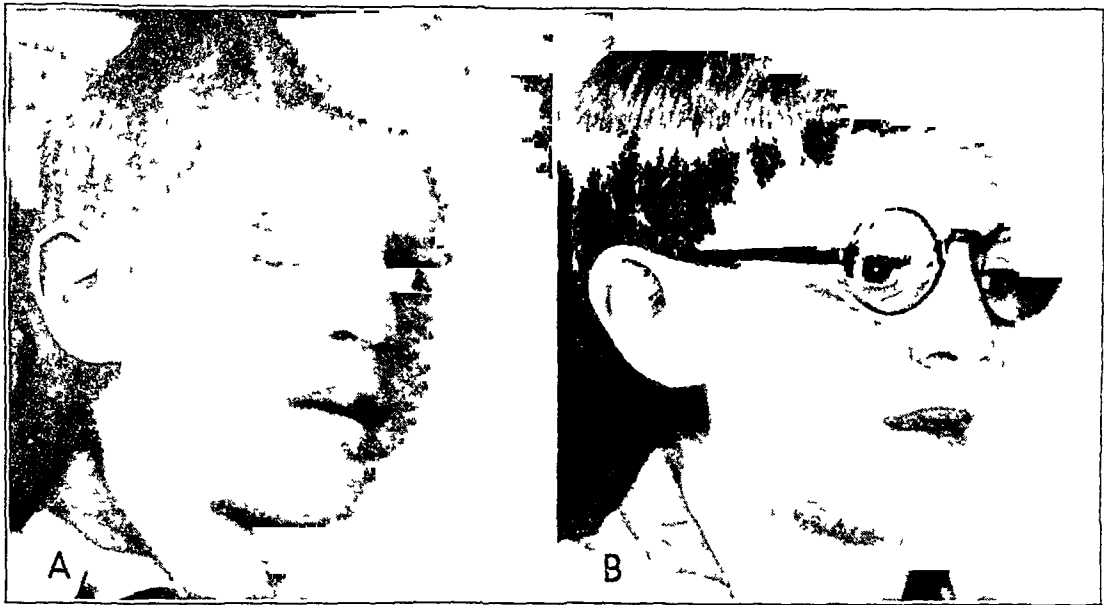


Fig 2—Four year old boy two years after surgical removal of the right orbit (A) without and (B) with prosthesis. Glasses disguise the edges of the restoration. A prosthesis furnished before a child reaches school age promotes confidence and goes far to stop the cruel taunts of schoolmates.

force trapped air to the surface. When the bubbles of air have been scooped off, the mixture is ready to be applied. It should be kept in contact with the surface to be molded for three or four minutes. While the impression is being made the patient should be reclining, and he should have been instructed to keep his eye fixed on a stationary point on the ceiling. Reassure the patient continuously during this procedure because the process tends to make the patient extremely nervous. I find that the more reassurance I give the patient the less muscular flicker results. Before removing the cast, be sure that the mold is firm and is not tacky. Do not hesitate to touch it with your finger after a few minutes to determine its firmness. When the consistency is satisfactory the impression is re-

hardens the molds and thus preserves the impression. The fixing solution may be painted or sprayed over the negative mold, or the mold may be immersed in the fixing solution. If the mold is small enough, it is always advisable to immerse it in the solution. To avoid distortion cotton padding should be placed on the bottom of the containing vessel. It is necessary to avoid contamination of other solutions with the fixing solution, therefore all solutions should be conspicuously marked. Generally, it is best to make a positive cast about an hour after fixing the mold. The negative should be separated from the positive impression about an hour after the stone becomes hard. As in all casting, it is advisable to use a type of dental stone or plaster with the least expansion and contraction. Also,



the compounds should be fine textured and hard surfaced. The technic for making a positive cast from a gelatinous negative mold is about the same as for making one from a plaster mold. The necessary amount of water is placed in a mixing bowl, and sufficient stone or plaster is added to absorb all of the water. The mixture is spatulated until it is smooth, and the bowl is tapped on the table or placed on a vibrator to eliminate bubbles. The top layer of plaster is then discarded, because it probably contains the undesired bubbles of air. The mixture is poured onto the negative mold from one side, so that it flows across the impression, this reduces the probability of enclosing pockets of air.

The hydrogen ion concentration of the gelatin compounds used for impressions of the eye should be within physiologic limits, and the

ing. Rather, a prosthesis should be considered merely as a substitute, an inconspicuous replacement for a missing organ. The ambition of the prosthetist should be not to create a striking example of sculpture but to make the patient's countenance as a whole as unobtrusive as possible.

The ensemble of the positive cast bearing the sculpture is next covered with freshly mixed plaster to form a two piece mold containing the sculptured restoration. When the plaster has hardened, the parts of the mold are separated, the sculpture is removed and the clay is washed out. The mold is thoroughly dried and is then ready for the construction of a pouring channel.

The pouring channel is usually made through the posterior portion of the mold or die. I find it best to make a conical channel with a diameter



Fig 3—Side view of the patient after surgical removal of the orbit (A) without prosthesis and (B) with prosthesis and glasses

mixture should be buffered. Control of the hydrogen ion concentration is effective in eliminating danger of injury to the eye and helps to lessen the patient's distress.

Ulcerated portions in the area to be covered by a prosthesis must be protected from contact with the prosthetic device, and it is sometimes essential that recently grafted skin be protected against contact with foreign material. This is especially necessary after ablation of carcinomatous tissue. Patients often apply for prostheses with the defective area still covered with friable, crusty, new skin grafts. Under such circumstances the positive cast must be altered by the addition of plaster to the area in which no contact is desired between the prosthesis and the skin. The positive cast and the needs of the patient should be carefully studied.

The operator should realize that his purpose is not simply to fashion a pretty organ that will be a neat and beautiful example of esthetic model-

ing. Rather, a prosthesis should be considered merely as a substitute, an inconspicuous replacement for a missing organ. The ambition of the prosthetist should be not to create a striking example of sculpture but to make the patient's countenance as a whole as unobtrusive as possible.

The ensemble of the positive cast bearing the sculpture is next covered with freshly mixed plaster to form a two piece mold containing the sculptured restoration. When the plaster has hardened, the parts of the mold are separated, the sculpture is removed and the clay is washed out. The mold is thoroughly dried and is then ready for the construction of a pouring channel.

The pouring channel is usually made through the posterior portion of the mold or die. I find it best to make a conical channel with a diameter of at least  $\frac{1}{4}$  inch (0.6 cm), to allow for easy pouring. Channels may be cut along the edge of the mold also, in such a way as to avoid altering the sculpture. It is a good rule to avoid channels which involve the anterior surface of the mold. If the mold is not thick enough or deep enough, it may be necessary to build an embankment of plaster around the pouring channels in such a way as to enlarge the cubical contents of the pouring channel. The flue must be large enough to contain enough rubber to keep the mold filled as the water is absorbed.

The amount of latex to prepare at one time varies with the number of prostheses one is about to cast. Because the zinc oxide that is added tends to hasten the coagulation time of the rubber, only a sufficient amount of the mixture to meet one's immediate needs should be prepared at a time. I usually prepare enough for several prostheses. I then divide the batch into



several small portions and color each for an individual prosthesis

From the mixture prepared for each prosthesis, it is wise to save a sample in a specimen mold or as scrap and to keep a record of the formula used. The record should state the type of latex used (including the trade name), the amount and type of filler, such as bentonite, starch or whiting, used and the formula for the color

#### Sample Record

Latex compound (trade name)	
Bentonite	1%
Zinc oxide	2%
D C red no 7 <sup>1</sup> } Suntan no 2770 <sup>1</sup> }	10%
(2 drops per ounce [30 Gm ])	

Such a record is of special value to the neophyte prosthetist, for as the record grows in size reference to it eliminates much disappointing trial and error in casting rubber

Once the rubber is prepared, it should be poured without too much delay. A piece of adhesive tape across the top of the beaker captures the air bubbles on the surface of the mixture and tends to prevent them from entering the mold. The rubber should be poured in a thin trickle or stream to permit the air in the mold to escape. If one desires a hollow prosthesis that is light in weight, the contents of the mold may be poured out again after about half an hour. This will leave a thin shell of rubber, with the interior empty. If the wall of the prosthesis is found to be too thin, the shell may be refilled after several minutes to build a thicker wall. Experience and the needs of the individual patient will help the prosthetist decide

whether to make the prosthesis hollow and delicate or solid and heavy

After the prosthesis is removed from the mold, it is left resting on one half of the mold for a day or so to permit the rubber to cure by contact with air. The flashing is trimmed off with a burning pencil and manicure scissors or a granite-grinding wheel. The glass eye is removed from the rubber eyelids, and with the thin blade of an electric burning pencil a groove is cut along the lower edge of the upper lid. Artificial eyelashes are fitted into this groove. Such lashes are supplied commercially in brown and black. After they are in place, the lashes are shortened and thinned with manicure scissors. It is not necessary to supply lower eyelashes. The glass eye is reinserted under the artificial lids, and the prosthesis is ready to be worn. It is glued in place with an adhesive containing gum mastic. Glasses may be worn over the prosthesis, but they are not necessary to support it. However, the edge of the lens and the temple bar tend to disguise the edges of the prosthesis.

If the patient reacts as most of mine have, after receiving his prosthesis he first displays it proudly to his relatives and intimate friends who know of his predicament. He receives compliments for the artistry of the restoration, admiration for his courage and friendly encouragement. If his morale is good, he displays his prosthesis in the same manner as normal people show their dental bridge work. After a few days he begins to meet strangers again, and his aim now is to keep the prosthesis as inconspicuous as possible. Therefore, the objective in sculpturing restorations is not to create a beautifully modeled part which attracts attention and admiration but to fashion a restoration that will permit the patient to fall back gratefully into the inconspicuous place he desires.

<sup>1</sup> Manufactured by the Kohnstamm Color Co., Chicago

# Clinical Notes

## AN ABSOLUTE MONOCHROMATIC OPHTHALMOSCOPE

JACOB B. FELDMAN, M.D., PHILADELPHIA

For the past three years I have used an absolute monochromatic ophthalmoscope of my own design and have compared observations with those made with the ordinary electric type. A spectroscope insures the monochromatic quality of the colors used in my ophthalmoscope.

Several hundred careful fundal examinations were made on normal persons as well as on those with pathologic conditions. These studies were temporarily discontinued<sup>1</sup> at about the time that a comparison of the fundal pictures as observed with my monochromatic ophthalmoscope with those obtained with the so-called "red-free"

with an exhaust fan and a holder (B) for the several filters: red, green, yellow, blue and ultraviolet.

The entire instrument is portable and can be used in any position and with ordinary alternating current. For fundal examination it is held in the hand as is the ordinary ophthalmoscope. The head (C) is taken from an old model De Zeng ophthalmoscope. A small model spectroscope is included with my instrument to insure the monochromatic quality of each of the filters used at the time of the examination of the eye-ground.

Of the various colors employed, green and particularly yellow gave interesting pictures, such as a clear view of minute blood vessels, exudates, hemorrhages and retinal nerve fibers.

### METHOD OF USE

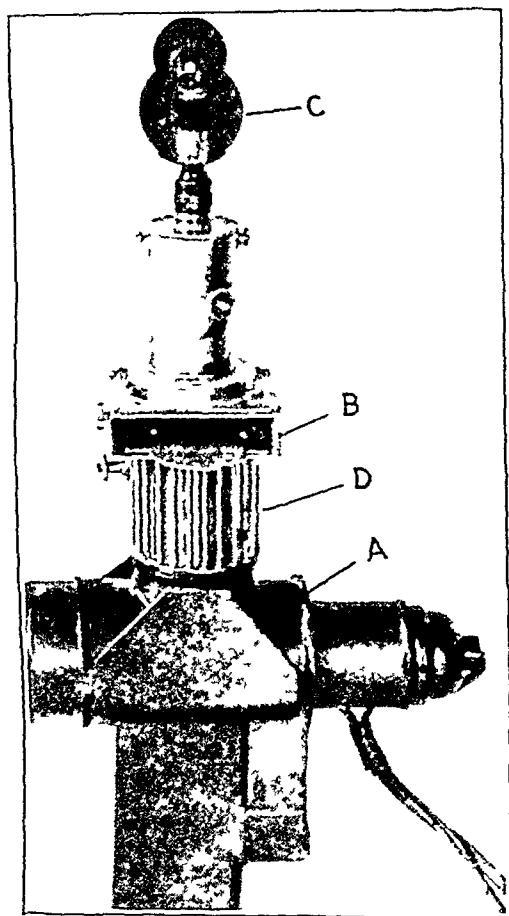
The light should be turned on for a minute before the instrument is used. The reason for this is that with the increase of the degree of heat generated by the light the maximum intensity of the color of the filter is obtained.

The next step is to insert the filter into the holder (B). It is imperative that unfiltered light never be used, or retinal damage will result. After the maximum intensity of color is obtained, the exhaust fan is turned on and the instrument is ready for use. If the fan is not turned on at about this time, the heat will become too intense and will extinguish the light. Five to ten minutes will then have to elapse before the instrument is cooled sufficiently and relit for further use. The multiple posts (D) safeguard the patient from an accidental burn.

### CLINICAL APPLICATIONS OF THE INSTRUMENT

It is well known that ultraviolet rays are an aid during the extraction of certain types of cataract. Some surgeons use ultraviolet rays only after operations for cataract to determine if all the matter of the lens has been removed. I have, however, found monochromatic yellow of greater value in illuminating the field after extraction of a cataract and during capsulotomy than either ultraviolet or intense daylight, which is generally used. It is possible that for the same reason the yellow color may be found of value in gonioscopy.

I am studying microscopic unstained pathologic sections of eyes illuminated with the



An absolute monochromatic ophthalmoscope

ophthalmoscopes now in general use was to be made. In this way it was hoped to determine what merit, if any, an absolute red-free ophthalmoscope has over the others in which colored filters are used without particular attention to their red-free quality.

The instrument consists of a lamp house (A) in which is incorporated a mercury vapor lamp

<sup>1</sup> Dr. Joseph I. Gouterman, medical corps, is now with the Armed Forces.

various monochromatic colors and comparing them with stained slides illuminated in the ordinary manner, to determine the relative merits of each process

The instrument is easily adaptable for any of the procedures which have been mentioned

The monochromatic ophthalmoscope may not entirely replace the regular ophthalmoscope for general use, but it will be of value in questionable fundal pathologic conditions by virtue of the fact that the color emitted absorbs certain colors in the retina, thereby making pathologic conditions stand out more prominently

## BILATERAL INFANTILE GLAUCOMA ASSOCIATED WITH BILATERAL HEMANGIOMA CONGENITALE (NEVUS FLAMMEUS)

### Report of a Case

A. M. RODIGINA, M.D.

Director of Eye Clinic, Izhevsk Medical Institute, Izhevsk, U.S.S.R.

I have had under my observation a case of an extremely rare condition, bilateral congenital hemangioma congenitale (nevus flammeus) associated with bilateral infantile glaucoma. A review of the literature and of the exhaustive bibliography cited by Ehrlich<sup>1</sup> have failed to reveal any case of a similar occurrence. It seems worth while, therefore, to report this case.

#### REPORT OF CASE

V. D., a boy aged 11 years had a dark red birthmark involving the scalp and the forehead except for a patch



Fig. 1—Bilateral hemangioma congenitale (nevus flammeus) associated with bilateral infantile glaucoma

of skin above the bridge of the nose. The birthmark extended downward to the left of the midline and involved the skin of the eyelid, the cheek, the nose and the upper lip, as well as the buccal mucous membrane and the palate. To the right of the midline the hemangioma involved the conjunctiva and the nose. The skin of the right cheek and the mucous membrane of the lips and the mouth showed no trace of the nevus

The birthmark characteristically followed the first two branches of the trigeminal nerve on the left side and the first branch on the right side (fig. 1). The contour of the lesion was highly indented. The localization of the birthmark had not changed since birth.

Vision was unimpaired until the age of 9, and the boy made good progress at school. Two years prior to his admission to the clinic the right eye became inflamed and painful. Vision became rapidly worse. During the last six months vision in the left eye deteriorated to a disastrous degree, and the boy had to discontinue attendance at school in the autumn of 1941.

The family history showed that his grandaunt had hemangioma congenitale.

**Examination**—The boy was well nourished and normally developed, the internal organs showing no departure from normal. The Wassermann reaction of the blood and the Mantoux reaction for tuberculosis were negative. The blood pressure was normal. A blood count and urinalysis revealed no abnormalities. Roentgenograms of the skull indicated no pathologic change in the sella turcica.

Both eyes showed great degeneration. The right eye was completely blind, with the left eye he could distinguish fingers at 0.5 meter.

**Right Eye** The eyeball was larger than normal along the anteroposterior axis, and projected anteriorly 3 mm in advance of the left eyeball. The nasal halves of both lids were involved by the birthmark, which then extended to the bridge of the nose. The conjunctiva of the lids and of the folds was slightly hyperemic. The conjunctiva of the eyeball and the episclera were reddish violet, especially around the limbus. Examination with a magnifying glass indicated that the cause of this lividness was the dilatation of a large number of conjunctival and episcleral vessels, the increased vascularity being especially prominent around the limbus, where the sclera thinned out. The cornea measured 13 mm in diameter, it bulged and showed a diffuse opacity. It was highly vascularized around the periphery. The vessels lay deep in the cornea, many being obliterated in places (as seen with the slit lamp).

The corneal sensitivity was impaired, and the anterior chamber was abnormally deep. The iris was dirty green and atrophic, the pupil was dilated and of irregular shape, with an uneven pupillary border, and did not react to light. The pupillary area was occupied by a cataract. The visual acuity of the right eye was

From the Eye Clinic of the Izhevsk Institute of Medicine

<sup>1</sup> Ehrlich, L. H. Bilateral Glaucoma Associated with Unilateral Nevus Flammeus. Report of Case. Arch. Ophth. 25:1002 (June) 1941.

zero The eye was as hard as stone The intraocular tension measured 65 mm of mercury (Schiotz)

Left Eye The eyeball was normal in size and shape The hemangioma involved the skin and conjunctiva The sclera of the lower half of the eyeball was abnormally thinned and was perforated by tortuous, dark red vessels, which projected on to the surface The cornea was 11 mm in diameter and was transparent, its

Systematic instillation of pilocarpine and physostigmine did not result in reduction of tension or improvement in vision Consequently, there was no hope of effective surgical intervention

The interest of this case lies in the fact that a bilateral hemangioma was associated with malignant bilateral infantile glaucoma, which had resulted in complete blindness at the age of 11

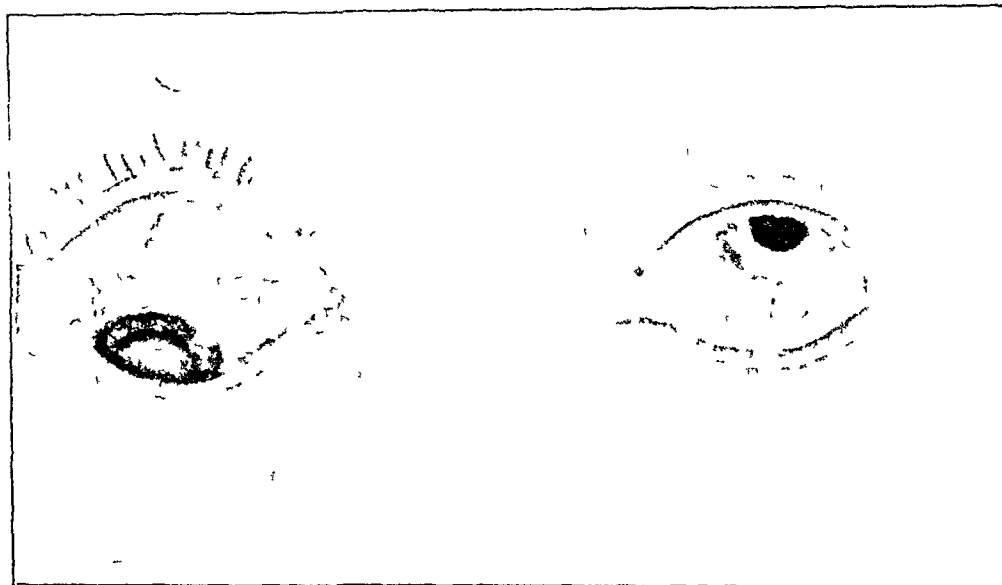


Fig 2—Appearance of the eyes in a case of bilateral hemangioma congenital associated with bilateral infantile glaucoma

sensitivity being less than normal The iris was light blue and of definite pattern The reaction of the pupil was sluggish to light The lens and the vitreous were transparent The papilla of the optic nerve was atrophic, the vessels being displaced toward the nasal edge of the papilla The arteries were hardly visible, only the veins remaining On the retina the veins were varicose and tortuous The choroidal vessels were not visible The tension was 45 mm of mercury (Schiotz) The visual acuity was 0.005 to 0.01

The cause of glaucoma in this case, whether it was dilatation of a blood channel in the tractus uvealis, i. e., a hemangioma similar to that of the skin, resulting in distention of the eyeball with fluid, or whether it lay in impairment of the sympathetic innervation, is difficult to determine It is certain, however, that there was a close connection between the glaucoma and the hemangioma and that both were congenital

Izhensk Medical Institute

## BIOMICROSCOPIC SURGERY AND TREATMENT

HOWARD E. CRAWFORD, M.D., HILO, TERRITORY OF HAWAII

Little has been written regarding the use of the slit lamp and the corneal microscope as an aid to ophthalmic treatment Berliner<sup>1</sup> mentioned their use in the removal of foreign bodies from the cornea This use became apparent to me several years ago, since many foreign bodies are so small that they can hardly be visualized by any other method Particularly in Hilo small spicules from the edges of sugar cane leaves commonly lodge in the cornea These penetrate into the stroma and are nearly transparent, consequently they can be seen only by direct and indirect retroillumination They may be multiple and can be removed only under magnification with the microscope Otherwise, they are absorbed slowly, with ocular disability lasting

from one to several weeks Any foreign body can be removed more precisely from the cornea by this method There is no need for excessive trauma The exact direction of force to be used is easily determined Small particles of rust, which are readily visible, can be removed with little difficulty

If it is necessary to cauterize an ulcer under the foreign body, or any ulcer for that matter, it is cleaned out by using a small applicator—a toothpick is about the right size—around which a tiny wisp of cotton has been tightly wound Such applicators should be sterilized in the autoclave prior to use The point is applied to the defect and twisted until the exudate is removed The chemical agent can be used on a similar applicator or on the bare wood and is applied exactly to the area over which cauterization is desired For the removal of foreign bodies

<sup>1</sup> Berliner, M. L. *Biomicroscopy of the Eye*, New York, Paul B. Hoeber, Inc., 1943, pp. 1-553

I prefer to use a 25 gage hypodermic needle which is fitted on the adapter of a Coakley antrum trocar for greater flexibility. Similar methods have been described previously.<sup>2</sup>

Before treating dendritic keratitis or corneal lesions resulting from other causes, it is often advisable to remove epithelium. This can best be done with a fine conjunctival forceps, although smaller pieces can be teased off with the needle.

Corneoscleral sutures, which are used in the extraction of cataracts, can be removed easily and accurately under biomicroscopic magnification. By ordinary methods it is easy to cut both sides of the loop and to leave a piece of silk buried. The exact application of the point of the scissors in the loop is not difficult under magnification.

Misplaced cilia can be removed easily. These are frequently light in color or broken and thus difficult to grasp unless magnified.

#### METHOD

The simplified universal slit lamp of Bausch and Lomb with standard magnification is the instrument which I use, but there appears to be no reason why others are not as good. The operator can use the right or the left hand, as preferred. The beam is directed from the side opposite the hand to be used, for instance, from the operator's left side if he expects to use the right hand. It is necessary that the hand be

steadied by resting it against the left side of the patient's nose and the left cheek when working with the right hand on the patient's right eye and against the side of the head rest when working on the left eye. It is frequently necessary to have an assistant hold the lids apart. Before the hand is put in place the patient's gaze is directed to the position desired and the microscope is focused on the point to be treated. The operator can then move away from the microscope, place the hand to be used in position and direct the instrument near the cornea within the beam of the slit lamp. He then moves back to the microscope, and the instrument, which can be seen through it, is slowly brought to the spot to be treated and the necessary manipulations carried out. In working on cilia, it is convenient to employ the free hand to manipulate the lid while the forceps is held in the other, the microscope having been focused before. When only one hand is occupied the other can be used for fine adjustments of focus, which are necessary occasionally when the patient moves. Diffuse illumination is usually all that is necessary for the treatment of foreign bodies, but for fine particles focal, direct and indirect illumination may be required, depending on their size and transparency.

#### SUMMARY

The use of the biomicroscope in ophthalmic treatment has not been sufficiently emphasized.

The magnification obtained by it permits accurate treatment of foreign bodies and ulcers and in certain instances is of value in the removal of sutures and cilia.

<sup>2</sup> Harding, G. F. Instrument for Removal of Foreign Body from Cornea, *Arch Ophth* **29** 134 (Jan) 1943. Appelbaum, A. Simplest Instrument for Removal of Foreign Body from Eye, *ibid* **30** 262 (Aug) 1943.

# Ophthalmologic Reviews

EDITED BY DR FRANCIS HEED ADLER

## DETACHMENT OF THE CHOROID

A CLINICAL AND HISTOPATHOLOGIC ANALYSIS

EDMUND B SPAETH, M D, AND PERCE D LONG, M D

PHILADELPHIA

The clinical condition commonly spoken of as detachment of the choroid is probably a more common manifestation of a pathologic process in the globe than is generally considered. The literature relating to it is remarkably scanty. Its treatment (when applied in any given case) is confused and too often of no consequence, and even its pathologic characteristics and its various etiologic and anatomic aspects are controversial. Rycroft<sup>1</sup> recently called detachment of the choroid "a poor relation of retinal detachment" and stated that as such it "occupies a position of insignificance in textbooks, where it is as often as not ignored entirely, or briefly dismissed with a few words." It is apparently not a distinct entity, seen only after operations for cataract and glaucoma. It occurs not only with perforating surgical procedures on the eye but as the result of severe trauma to the eye, it may be either hemorrhagic or nonhemorrhagic, and it appears as a terminal phase in pathologic conditions of the uveal tract.

We believe that the underlying pathologic process in the choroid is the same regardless of whether the condition is serous or hemorrhagic or both, and that the immediate cause may be connected with (a) an intraocular surgical procedure, (b) traumatic perforation of the globe, either of the posterior or of the anterior segment, (c) trauma to the globe, without perforation, or (d) inflammatory changes, which may be acute but usually are chronic and of long standing.

In the examination of microscopic sections in connection with this study, it was necessary, first, to decide with reasonable exactness what constituted a pathologic condition and to what degree choroidal and perichoroidal separation

are present not as the result of fixation and staining of the tissue (artefacts) but because of disease or of faulty intraocular mechanical situations. Many wholly normal eyes show some separation of the perichoroidal space from the sclera (even up to the ora serrata), with the suggestion of an albuminoid material lying between the choroid and the sclera—breaking up the perichoroid into lamellas—certainly only an artefact. Many sections examined had to be rejected for this reason, as not demonstrating pathologic detachment of the choroid. Our criteria for the presence of a pathologic process were the degree of apparent lamellar formation and separation, the constant presence of an interlamellar, a subretinal or a subchoroidal fluid which coagulated with the fixative and took a stain<sup>2</sup>, the presence of cellular elements and other signs of trauma or of inflammation, such as red blood cells, dilated blood vessels and round cell infiltration, contiguous or adjacent lesion of the retina, and pathologic changes between the choroid and the sclera. Figure 1 illustrates the formation and separation of choroidal lamellas, a change which is probably largely an artefact. The section is from the choroid of an enucleated eye, removed because of progressive keratitis with long-standing endocyclitis. The walls of the vessels are thickened. Chronic inflammatory areas lie immediately beneath the pigment, and the greatest formation of choroidal lamellas lies, properly, in the deeper layers of the choroid, close to the sclera. In this eye the retina showed an area of old degeneration and was completely detached. The picture in figure 2 was also considered within the normal. The eye had been enucleated because of continued, intractable hypertension with blindness. A few superficial hemorrhages lay in the choroid. The alterations in the choroid extended toward the left as a rapidly narrowing area of splitting

From the laboratory and clinical services of Wills Hospital.

Dr Bernard Samuels and Dr T L Terry gave assistance in the preparation of this paper, and Dr Arnold Knapp made suggestions and offered constructive criticism.

<sup>1</sup> Rycroft, B W Choroidal Detachment, Brit J Ophth 27 283, 1943

<sup>2</sup> O'Brien,<sup>9</sup> citing Reese, discussed the supra-choroidal space, which normally contains a small amount of transudate and, therefore, is to be regarded as a lymph space.

of its structure, which undermined the ciliary body and freed it from the sclera. Figures 1 and 2 therefore illustrate a minimal pathologic change, the condition of the choroid, however, is probably not the true choroidal edema of the

us (E. B. S.) discussed at length with Dr. Bernard Samuels the mechanics of detachment of the choroid. Dr. Samuels was closely associated with Ernst Fuchs in histopathologic studies. He (Samuels) contributed generously

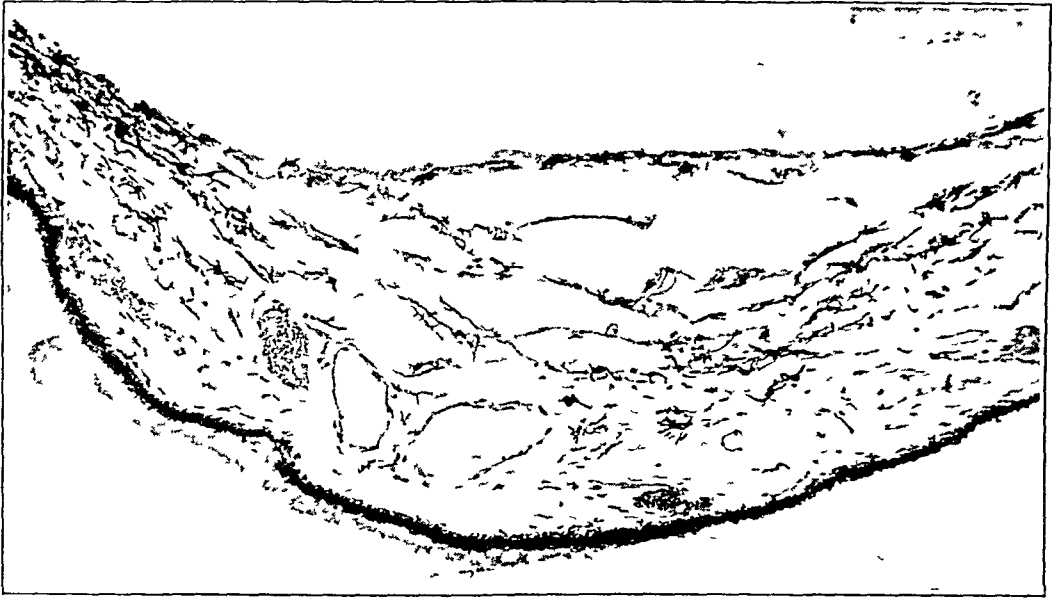


Fig 1—Lamination of the perichoroid, considered as an artefact

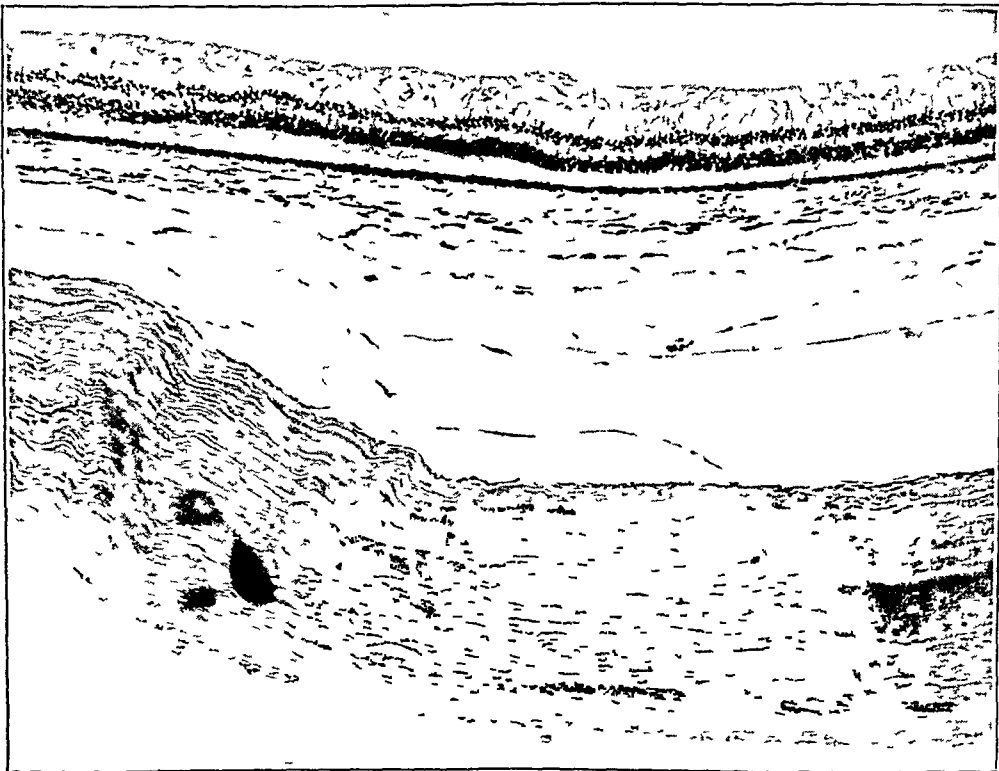


Fig 2—A situation similar to that in figure 1

type under discussion. Figure 1 represents, perhaps, a borderline condition.

While we were engaged in the extensive and time-consuming study of many microscopic slides in the laboratory at Wills Hospital, at the suggestion of Dr. Arnold Knapp, one of

from his notes and his personal memories of Dr. Fuchs's comments on this subject and gave us access to a large number of slides from the Hofrat professor's original preparations. The opinions expressed by Dr. Samuels were borne out by our observations. It was gratifying

also, that our conclusions, as expressed in the second paragraph of this paper, closely parallel those stated years ago by Fuchs

Actually, as has been reported frequently in the ophthalmologic literature, Dr. Heiman Knapp was the first to see and record a detachment of the choroid. After an operation for cataract, he saw a dark, semiglobular projection in the vitreous body and mistook it, naturally, for a melanotic tumor. The eye was enucleated, and subsequent microscopic examination showed that the true condition was a "serous detachment of the choroid." Doi made the same mistake in 1934, but in a case of late choroidal detachment, occurring two months after corneoscleral trephining.

In many cases detachment of the choroid whether or not it is suspected cannot be seen during life because, for various reasons, the interior of the eye is not accessible to ophthalmoscopic study. Perforation of a globe after an ulcer, with sudden diminution of intraocular tension, or a massive hemorrhage into the vitreous due to trauma to the eye but without perforation are instances of such conditions.

Fuchs first expressed the conviction, which has recently been confirmed by O'Brien, that detachment of the choroid occurs frequently after operation for cataract. The incidence is high in cases in which the anterior chamber does not refill for a long time after the operation. One wonders and logically whether failure of the anterior chamber to reform may not be the result of a choroidal detachment (if so, a reversible process), rather than the choroidal detachment's being the result of the delayed reformation of the anterior chamber. If so, and in these instances, the choroidal detachment must have occurred before the reformation of the anterior chamber could play any role in its production. It is a fact that the choroid seldom becomes detached in cases in which the anterior chamber has once been reformed within a normal period, without event or previous complications, and the chamber is subsequently emptied as a result of incidental trauma. It may be that in such cases the choroidal arterioles and capillaries have already become conditioned to lower pressure levels, and hence the frequency of detachment is much less.

Certainly, after corneoscleral trephining detachment of the choroid is common. Actually, it seems, clinically at least, to be most common after this operation. This may be only apparent, since the fundus is usually examined earlier after operation for glaucoma than after cataract extraction. In cases of glaucoma the relation of preoperative hypertension, continued postoperative hypotension, failure of the anterior

chamber to form again and duration of the choroidal detachment is interesting. Fuchs<sup>3</sup> commented that detachment of the choroid seldom, if ever, follows cyclodialysis. This observation is true with respect to serous detachment of the choroid, but not with respect to the hemorrhagic form. Also, Fuchs observed that choroidal detachment was much more frequent after iridectomy for acute glaucoma, and this statement seems to be supported by our present observations and by the results of our routine postoperative examinations. Fuchs described the condition in 11 cases after 14 iridectomies for acute glaucoma<sup>4</sup> (also cited by Rycroft<sup>5</sup>). According to Fuchs's earliest theory a rent in the perichoroidal space was necessary for the development of the detachment. A case will be presented later in which detachment of the choroid persisted for weeks after a corneoscleral trephination, the external wound healed completely but external filtration was not set up and the anterior chamber did not reform. External filtration through the operative trephine opening did not become established until the choroidal detachment had disappeared. It seemed that a posterior subchoroidal drainage, toward the vortex veins, was the reason for the hypotension and that when this ceased, the anterior chamber reformed and external filtration took over the drainage. It is a fact also pointed out by Fuchs, that the regions of the vortex veins themselves, in cases of the serous type of detachment, are not involved and that they limit the detachment, as though the veins bound down the choroid at their points of exit. This observation, hence, makes it permissible to wonder whether in such cases the presence of a choroidal detachment may not equally as often be the cause as the result of failure of the anterior chamber to reform. The situation is almost *post hoc, ergo propter hoc*.<sup>5</sup>

With the usual choroidal detachment following an operation for cataract, one can see, behind the plane of the pupillary aperture, with and sometimes without the ophthalmoscope, a smooth gray, semiglobular elevation, displaced somewhat to the temporal or to the nasal side. Such a lesion is to be differentiated from a detachment of the retina by its darker color and by the absence of folds or undulations. As the wound closes and the anterior chamber is refilled, the detachment disappears spontaneously regardless of any so-called methods of treat-

3 Fuchs, E. Ablosung der Aderhaut nach Operationen. Arch f Ophth 53 395, 1902

4 Fuchs, E. Ablosung der Aderhaut, Arch f Ophth 51 199, 1901

5 To wit the fallacy of arguing from mere temporal sequence the relationship of cause and effect



ment The explanation of the mechanics of its formation, according to Fuchs, is as follows

When part of the contents of the eyeball is evacuated, as in a lens extraction, its loss may be compensated for by the entrance of air into the eye, or the scleral capsule collapses, by reason of its elasticity, to the extent which is necessitated by the diminution in the contents of the eye When, however, this elasticity is insufficient, atmospheric pressure is transmitted through the orbital fat The sclera has a tendency to resume its original form, as does a compressed rubber ball As a rubber ball, when freed from the pressure of the hand, has the property of producing suction, so the rebound of the sclera causes a negative pressure to become operative in the interior of the eye, in consequence, there is a

suprachoroiditis, without, however, rupture of the retina or the internal limiting membrane of the retina, was seen recently after a basal iridectomy for glaucoma Transscleral drainage confirmed the hemorrhagic origin The other extreme is seen in cases in which the hemorrhage is so tremendous that the choroid is forcibly pushed against the vitreous body, the vitreous is then expelled from the eye, and the retina and the choroid follow The mechanics operative here does not differ much from that producing choroidal detachment after operation, but without hemorrhage When the vessels of the

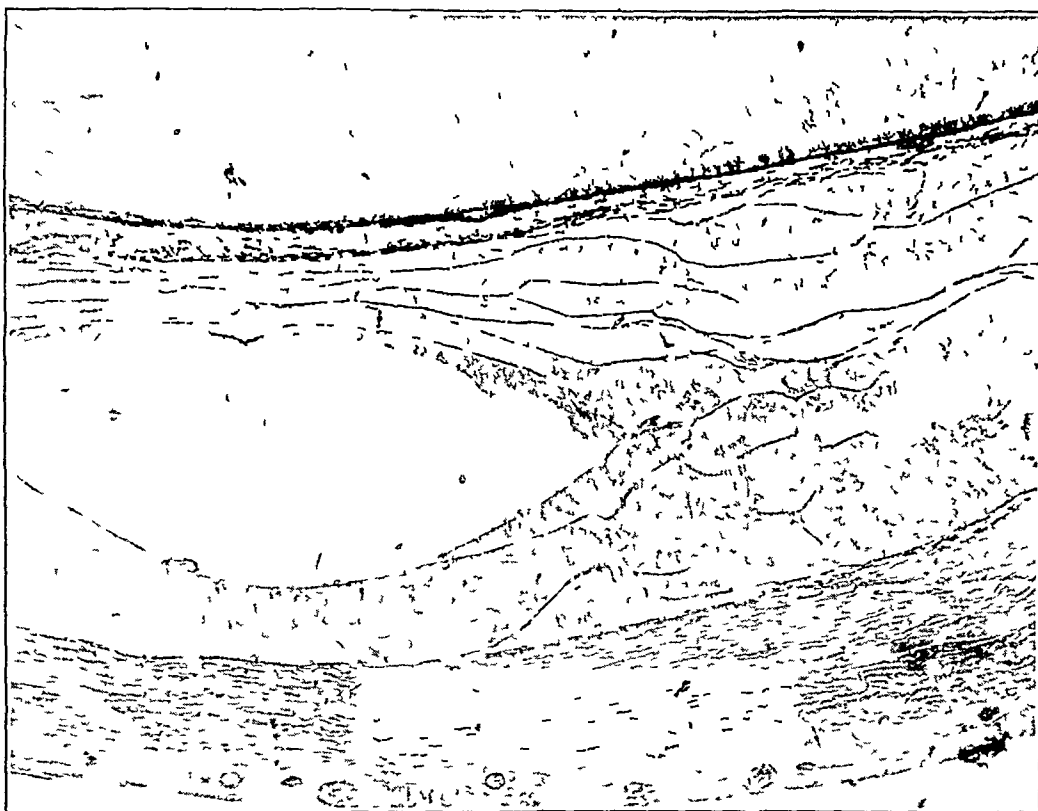


Fig 3—Enucleation following severe trauma to the globe

transudation of serum under the choroid In proportion to the increase in the intraocular pressure as it regains its normal level, this serous detachment decreases, owing to the absorption of the fluid beneath it With the closing of the wound in the eye, fluids within the vitreous cavity form again to raise the intraocular tension to its former pressure<sup>6</sup>

This form of choroidal detachment is the first type in Fuchs's classification

Fuchs's second type of choroidal detachment is the hemorrhagic, or the so-called expulsive, hemorrhage All degrees of severity of this type may be seen As an example, hemorrhagic

<sup>6</sup> This quotation, as well as the discussion of the four types of detachment, is a contribution to this study by Dr Samuels Corroboration with him emphasizes that close rapport which exists between surgery and histopathology

choroid are suddenly released from the external normal or increased pressure (as in cases of glaucoma) to which they have become conditioned, a greater quantity of blood enters them than they can hold, as a result they burst A slide in Fuchs's collection showed the following condition After perforation of a serpiginous ulcer in a case of glaucoma, there had escaped through the aperture, and lay in front of the eye, though still attached to it, a large sac filled with blood, the walls of the sac being formed by the everted prolapsed choroid (Samuels)

The third type of choroidal detachment of the choroid described by Fuchs is the form seen frequently in atrophic eyes Apparently, the cause is similar to that of detachment of the retina seen frequently in the same eyes, namely,

traction due to cyclitic membranes. The lens becomes pressed against the cornea by these membranes, which include the ciliary processes, only in microscopic sections because an ophthalmoscopic examination cannot be made. The extent of the detachment is occasionally so great

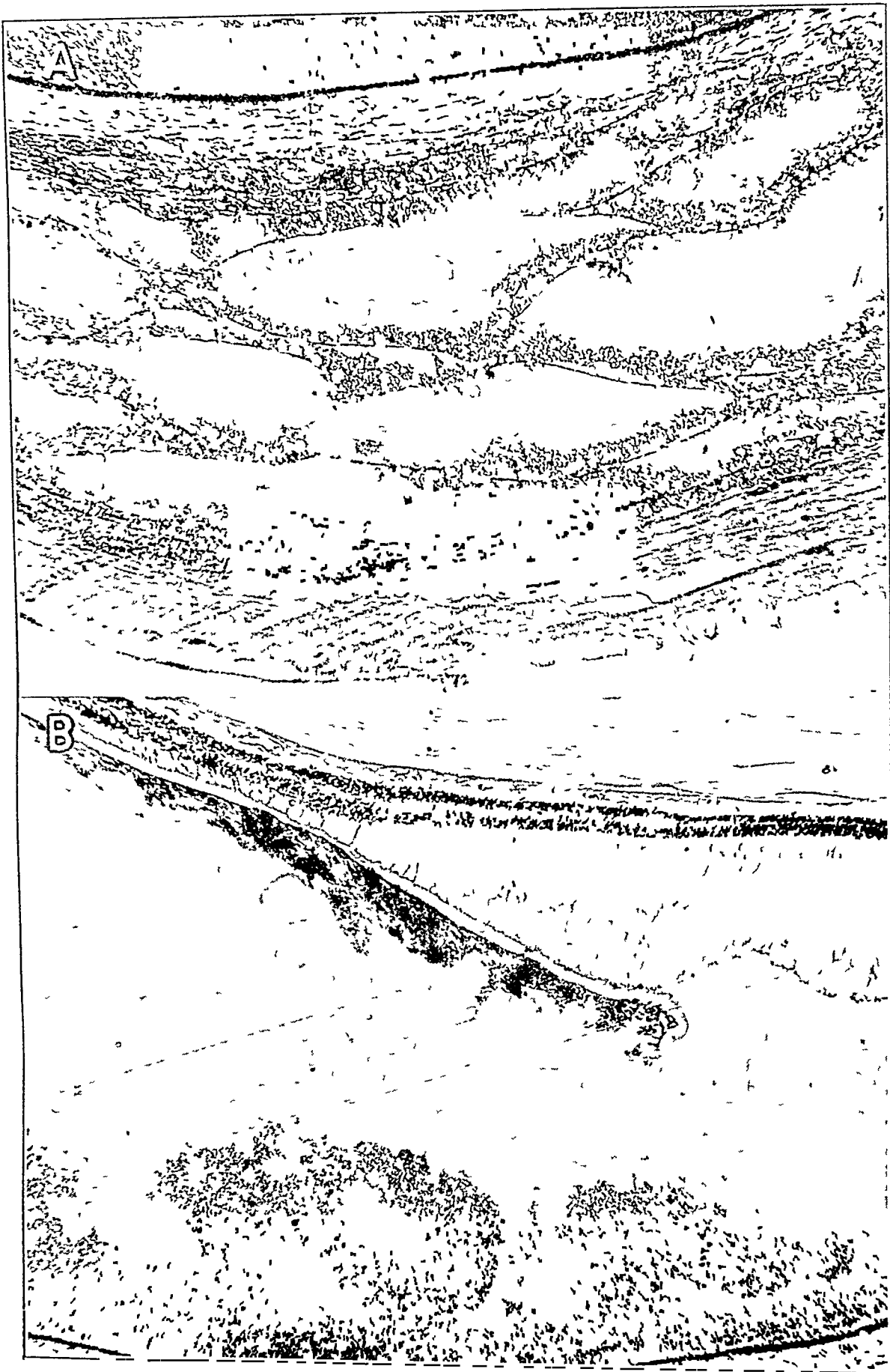


Fig 4—Traumatic rupture of the globe

so that there is pulled toward the anterior portion of the eye a conglomerate mass composed of the ciliary body, the retina and the layers of the choroid. This form of detachment can be seen

that the choroid, as a result of its own hydrops, as well as the general shrinkage of the globe, is many times as thick as normal. In this type of detachment, the choroidal fragmentation is

most conspicuous, and a densely staining interlamellar albuminoid fluid is present

The fourth type of detachment, according to Fuchs,<sup>3</sup> is produced by the transudate present in an acute inflammatory process. Microscopic sections showing such a condition are not common, one such section was studied with Samuels, in which severe endophthalmitis followed a perforating injury, with formation of pus in the anterior chamber of the eye. Besides the periretinal exudates, which lay free, as well as in patches, in the vitreous, on the inner surface of the retina and in the choroid, there existed at one spot a large amount of transudate between the choroid and the sclera.

three subtypes immediate, delayed and spontaneous. We feel that the so-called spontaneous detachment of Meller is an inflammatory condition, his immediate and delayed forms are also discussed in this paper under other heads.

#### CHOROIDAL DETACHMENT OF HEMORRHAGIC ORIGIN (CLASS 1)

There is no doubt that complete detachment of the choroid from the sclera may occur. The inverted choroidal sac, prolapsed after an intra-choroidal expulsive hemorrhage, illustrates the possible completeness of this detachment. Usually, however, the detachment of the choroid itself from the sclera is minimal, perhaps only in



Fig 5—Old penetrating wound of the eyeball, with secondary glaucoma

It is interesting that since the beginning of the present study, Rycroft<sup>1</sup> has called attention to a subdivision of which we were unaware.

Barkan lists four classes of choroidal detachment:

- 1 Tear of the ciliary body with the aqueous percolating into the suprachoroidal space (Simple type)
- 2 Traction on the choroid and retina by organizing masses in the vitreous (Traction type) [fig 13]
- 3 Sub-choroidal haemorrhage (Degenerative type) [fig 9]
- 4 Massive choroiditis with sub-choroidal exudate (Inflammatory type) [fig 11]

In Meller's<sup>7</sup> classification (also cited by Rycroft<sup>1</sup>) Fuchs's first type was divided into

places, as can be seen in figure 6 B. Apparently, the process starts with traumatic rupture of one of the larger choroidal vessels. With continued bleeding, the perichoroid is split off from the sclera below through an extensive dissecting hemorrhage. In some cases the process may be self limited at this point, in others, as a result of continued bleeding, there occur perforations of the choroid, retinal detachment by the hemorrhage and even massive preretinal hemorrhages into the vitreous undoubtedly passing through the retina.

Figures 3 to 7 illustrate such hemorrhagic forms.

Figure 3 is from an eye enucleated after severe trauma to the globe, followed by pain and blindness.

<sup>7</sup> Meller, J. Ueber postoperative und spontane Chorioidealahhebung, Arch f Ophthn 80 170, 1911

The globe was not ruptured. The section shows traumatic choroiditis with edema and the formation and extensive fragmentation of perichoroidal lamellas. The lamellas are separated from each other by a large amount of blood pigment. A large space indicates where a blood clot has fallen from the section. The greatest pathologic change is in the deeper portion of the choroid, the portion lying next the retina being less involved. A retinal separation appears in the upper part of the section. A subretinal transudate takes a dense stain.

Figure 4 is from a case of traumatic rupture of the globe. *A* shows massive edema of the choroid, with fragmentation and the formation and separation of choroidal lamellas, i. e., a suprachoroidal pathologic process, largely hemorrhagic. The perichoroidal fluid is in part serous and in part hemorrhagic. In *B*, another section from the same eye, the pathologic process in the deeper part of the choroid is largely hemorrhagic, with extensive hemorrhages, which are suprachoroidal as well, and densely staining albuminoid material. The retinal changes are profound. In this section transudation is an outstanding characteristic, being not only choroidal but preretinal.

Figure 5 is taken from a case of an old penetrating wound of the eyeball with secondary glaucoma. The edema of the choroid here is interesting in that, with the blood between the perichoroidal lamellas, it is perhaps responsible for the fragmentation and separation of the perichoroid. In this eye there were small areas of retinal separation, with small preretinal hemorrhages. The separation of the retina was most pronounced at the ora serrata. The greatest degree of hydrops seen in this hemorrhage-filled choroid was about the papilla, the edema extending laterally, toward the normal choroid.

Figure 6 is from a case of impact trauma to the globe without perforation. *A* is a photograph of the entire eye. *B* shows regions in which the choroid has apparently been lifted by the massive intrachoroidal hemorrhages, with edema when it was freed wholly from the sclera. *C* is a section taken from the uppermost part of the suprachoroid, the blood clot lying immediately behind the matted, detached retina, posterior to and slightly below the posterior pole of the lens. Careful scrutiny of *6A* will show the site of this section. The superior portion of *C* shows remnants of choroidal structure. The lower portion contains no remnants of choroidal structure.

Figure 7 is a section from an eye with old hemorrhages following an operation for glaucoma. The picture suggests the possibility of a former expulsive hemorrhage. The section shows no choroidal tissue as such—simply dilated vessels, round cell infiltration, many larger cells, which appear to be epithelioid, and blood pigment. The picture is probably one of late organization after subchoroidal or intrachoroidal hemorrhage. An extraocular hemorrhage below, outside the sclera, was probably associated with the enucleation. It seems hardly to be part of the intraocular process. The globe failed to show the presence either of the choroid or of the retina. They were undoubtedly expelled with the hemorrhage.

These microscopic sections of hemorrhagic situations are traumatic and postoperative and illustrate the second type of Fuchs's classification,

that is, choroidal detachment of a hemorrhagic type.

The following 2 cases are illustrative of this form.

Case 1 is apparently an instance of pure choroidal hemorrhage.

CASE 1—R. H., a man aged 20, when at a seashore resort with some companions was skylarking on a dock, approximately 20 feet (6 meters) from the water. He was pushed from the dock and struck the water on his face and chest. When he came from the water, it was seen that multiple subconjunctival hemorrhages were developing in the right eye. Examination of the fundus within an hour, through the dilated pupil, showed a dome-shaped elevation, starting at the equator and rising steadily to about 10 D at the ora serrata. There were a few fine capillary hemorrhages in the retina over this elevation and several somewhat grosser ones in the otherwise normal retina contiguous to the elevated edge of this area. The rapidity of its development, the absence of any movement in the elevated area and the failure to find a retinal tear suggested a choroidal hemorrhage. The rapid and prompt subsidence of the entire condition, beginning within four days, made the diagnosis of retinal separation impossible. Some of the hemorrhages were still apparent on the retina when the patient was last seen, on the fourteenth day after the accident. The appearance of the fundus and the prompt subsidence of the pathologic process made impossible any diagnosis but that of choroidal hemorrhage.

In case 2 the hemorrhage not only was between the retina and the choroid, with perhaps considerable secondary edema, but was subchoroidal. The subsequent progress of the condition suggested that the choroidal hemorrhage originated from the simultaneous rupture of at least three of the four vortex veins of the choroid. This case illustrates beautifully the observation made by Verhoeff,<sup>8</sup> cited by O'Brien,<sup>9</sup> that angioid streaks in the choroid almost certainly indicate a previous separation of the choroid. The detachment in this case was accompanied by little, if any, primary retinal separation.

CASE 2—C., a Negro boy aged 5 years, was struck in the left eye by the end of a broom handle. He was admitted to the hospital with severe edema of the conjunctiva and with the entire anterior chamber of the eye black with clotted blood. The sclera was not ruptured. A severe exophthalmos, present on admission, receded rapidly. The blood clot in the anterior chamber began to absorb, and on the tenth day after his admission one could see a massive elevation of the entire fundus. The optic papilla was visible in the depths of this funnel-shaped area. Multiple hemorrhages, many of them gross, were scattered over the surface of the retina. No retinal tear or disinsertion could be noted, even through the dilated pupil and

8 Verhoeff, F. H. Nature and Origin of the Pigmented Streaks Caused by Separation of the Choroid, *Tr. Sect. Ophth., A. M. A.*, 1931, p. 82.

9 O'Brien, C. S. Detachment of the Choroid After Cataract Extraction, *Tr. Am. Ophth. Soc.* 33:325, 1935.

with external pressure exerted at the limbus. The patient was given pinhole glasses, and was placed under treatment with atropine and dehydration. Transillumination from the depths of the orbit showed large, patchy areas of well defined shadows. The working diagnosis was that of massive, irregular choroidal hemorrhages, without rupture of the globe. The condition slowly and steadily receded without any treatment other than that mentioned. The recession of the process was interesting in that the areas of initial impairment noted with transillumination at the site of three of the vortex veins remained evident for some time, well on to six weeks. Between these areas the retina, now atrophic, receded to a normal position. The hemorrhages on the surface of the retina disappeared. The grayish pink of the normal fundus of a Negro boy was lost and was replaced by three radiating areas of massive angioid streaks, outlining respectively a large greenish area in the superior nasal region, a similar large inferior temporal area and a somewhat smaller, but similarly colored, inferior nasal area. Vision was lost entirely, as a result of the high degree of secondary atrophy of the retina, which was apparently due to the extreme damage to the choroid. The nerve head was entirely atrophic.

Case 3, also one of traumatic detachment, illustrates a slightly different type of damage, the retinal process in this instance not being hemorrhagic.

CASE 3—R. B., a boy aged 6, was struck on the left eye, apparently through the upper lid, by an arrow shot from a toy bow, at a distance of about 15 feet (4.6 meters). The boy was seen within an hour after the accident. There was a small laceration in the midline of the upper lid. The pupil was pinpoint. There was a crescent of blood cells in the lowest part of the anterior chamber, its greatest height being 2 mm. Visual acuity was grossly impaired but was not measured. The pupil was dilated with atropine. When the patient was seen six hours later, the entire anterior chamber was filled with fresh hemorrhage, a third hemorrhage occurred twenty-four hours later. These hemorrhages absorbed rapidly, so that the fundus could be seen by the fifth day after trauma. At that time the entire macular region was raised, the elevation measuring about 6 D., the area was dome shaped and gray, with a pink center, which was slightly dimpled, in fact, the picture was that of the classic edema of contusio bulbi, though of unusually severe degree. There was rapid and steady recession of the pathologic process. In ten days vision with atropinization was 6/12, and pinhole vision was 6/5. The patient made a complete recovery.

The condition in this case must be considered as pure retinal edema. The anatomic distribution of the retinal and choroidal capillaries predisposes to pure macular edema in cases of such contusions. When central retinal necrosis occurs after trauma (as in a case of a hole in the macula), it suggests a pure retinal condition. The bright red appearance of the intact choroid, as seen ophthalmoscopically through a hole in the macula, confirmed the integrity of the choroid, with destruction of the overlying retina. The hemorrhages in the anterior chamber had probably nothing directly to do with the changes in

the posterior segment. The time element, that is, the prompt recession and the rapid recovery of central visual acuity, was definite evidence against the presence of any choroidal hemorrhage.

The circulation of the choroid, as presented by Leber,<sup>10</sup> suggests that pure choroidal edema should be least common and least severe at the posterior pole of the eye, it should be much more frequent and more severe at the anterior periphery, that is, as the region of the ora serrata is approached. It is interesting that this assumption is usually borne out clinically.

Case 3 is presented as representative not of a choroidal but of a pure retinal condition, relevant to the subject only as it offers a contrast to the various factors, anatomic and mechanical, emphasized in the first 3 cases.

Of necessity trauma to the eye without perforation which results in rupture of the choroid

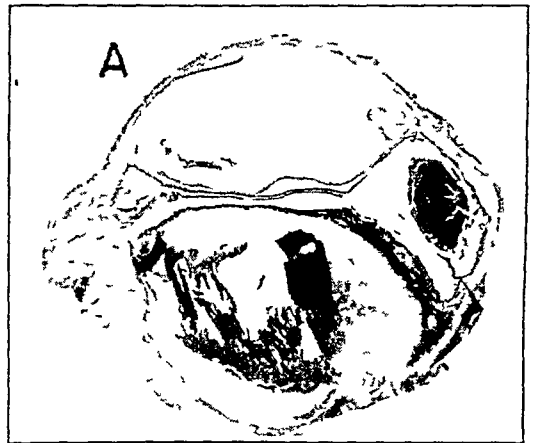


Fig 6—Impact trauma to the globe without perforation

means hemorrhage. Direct trauma, with or without rupture of the choroid, but with disinsertion or laceration of the retina, results in separation of the retina, regardless of whether there is accompanying choroidal hemorrhage. In cases of trauma, both perforating and nonperforating, with retinal separation the immediate cause and/or accompaniment may be choroidal, retinal or subretinal hemorrhage. It is likely that the retinal separation would not persist unless pre-retinal elements, such as the vitreous and serum, found entrance into the subretinal regions through a laceration or disinsertion of the retina, with separation of the retinal layers from each other. This source of retinal detachment within the retina is commonly recognized. The two possible results of trauma offer an interesting study. From similar causes dissimilar and

10 Leber, T. Anatomische Untersuchungen über die Blutgefäße des menschlichen Auges, Vienna, 1865

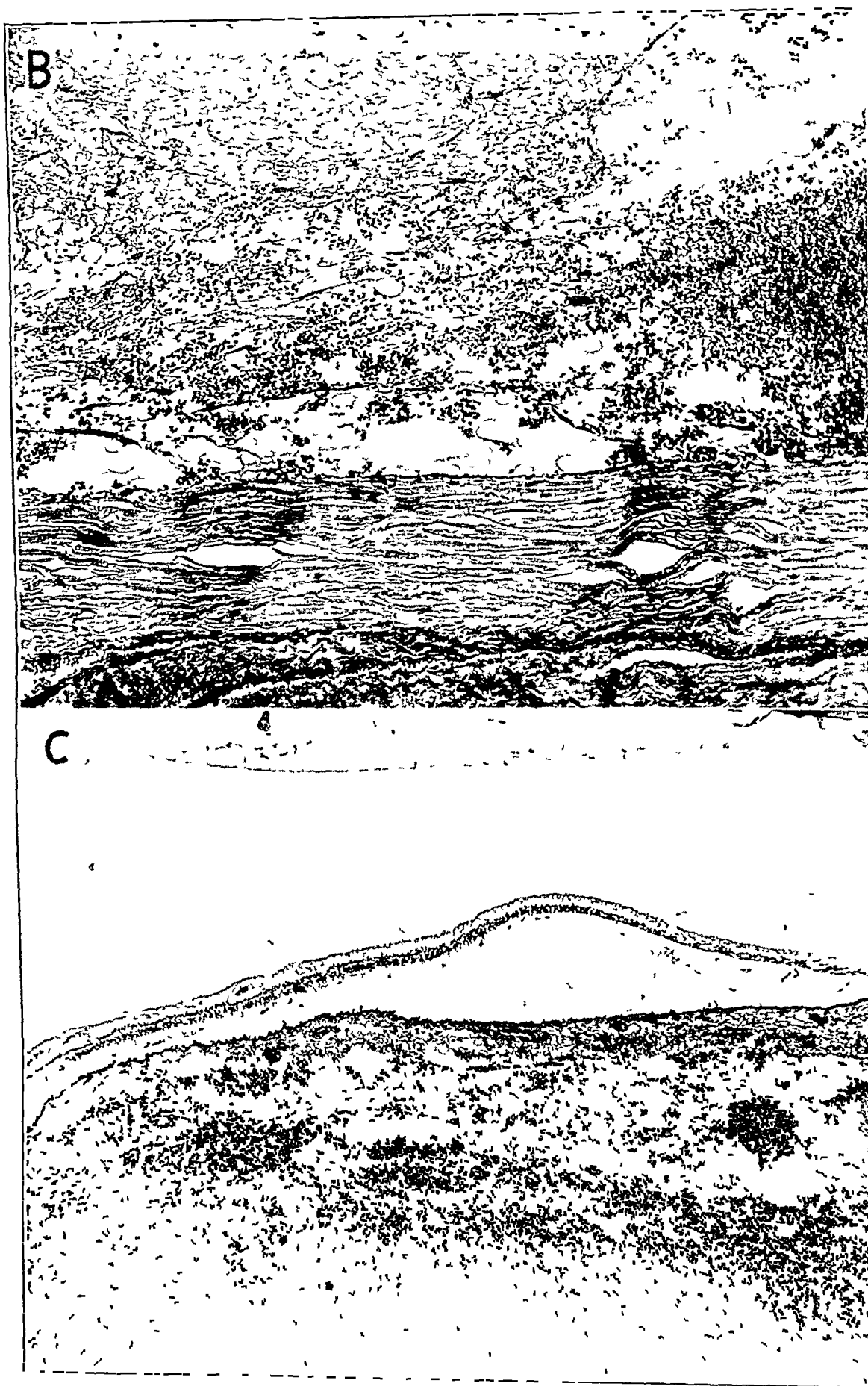


Fig 6 B and C—See legend on opposite page

permanent anatomic changes and end results may develop. This is not uncommonly seen clinically. It is disheartening to find that after absorption of a large preretinal hemorrhage in the vitreous (which up to that time has obscured the ophthalmoscopic details) the patient has as well an extensive retinal detachment. In such a case the interval which has elapsed before the diagnosis could be made has been so long that the chances of any satisfactory surgical repair of the retinal separation are almost nil.

Samuels,<sup>11</sup> in discussing the anatomic conditions connected with nonexpulsive subchoroidal hemorrhage, that is, the hemorrhagic form of choroidal separation, stated

The amount of blood may be just enough to cause a low circumscribed detachment of the uvea far forward or it may be so large as to undermine the uveal tract on one side, from the scleral roll anteriorly to the margin of the optic nerve. [This is well illustrated in case 2 presented here. Instead of the long posterior ciliary artery's being ruptured in that instance, however (see later discussion), the three areas of opacity, the results of transillumination and the subsequent progress of the condition made it more likely that three vortex veins had been ruptured.] Usually the blood does not undermine beyond the limit of the perichoroidal space. As this comes to an end posteriorly at a considerable distance from the nerve head, it is exceptional to find blood under the choroid in the posterior segment of the eye. The vortex veins superiorly and inferiorly fix the choroid to the sclera [as Fuchs formerly stated], in the region of the equator. For this reason the blood clot accumulates on the nasal or temporal side, where there is nothing to prevent the choroid from detaching itself from the sclera. The retina remains adherent to the choroid in all cases, because both layers are compressed against the vitreous body.

Samuels expressed the opinion that the bleeding comes not from the choroidal vessels themselves but from a rupture of one of the two long posterior ciliary arteries. The seat of the rupture is probably at the site of entrance of the artery into the perichoroidal space. In several of his specimens fragments of the walls of this vessel were observed clinging to the emissarium. In 1 case the adjacent stroma was infiltrated with blood which had found its way there from the perichoroidal space. The distal walls of the ruptured vessel retract and degenerate, so that they no longer can be seen in the blood clot.

In comparing choroidal detachment due to the extravasation of blood and choroidal detachment due to transudation of serum, Samuels stated<sup>11</sup>

Extravasation of blood takes place rapidly, the transudation of serum develops slowly. Both are found in greater accumulation forward in the region of the ciliary body. A transudation is confined to the normal limits of the perichoroidal space, while a hemorrhage may undermine the choroid as far as the optic nerve

[see case 2]. The two do not occur together. Bleeding, coming on abruptly, leaves no time or space for the transudation of serum. Eyes showing hemorrhage under the choroid are hard, those showing serum are soft. A fibrous thickening of the suprachoroida persists after the disappearance of blood, but no membrane is found after the absorption of a transudate.

The following case is illustrative.

CASE 4—Mrs. R., aged 64, had bilateral cataract. An uneventful intracapsular extraction of the lens was done on the right eye. Some time later a similar operation was performed on the left eye. This operation, a simple extraction, was performed with the patient under anesthesia induced with solution of tribromoethanol, a peripheral iridectomy being made immediately after the section, and prior to extraction of the lens. This of itself was uneventful. Two conjunctival sutures were inserted after the section. As a dressing was about to be placed over the eye, one could see vitreous trickling from the external canthal angle. The lid sutures were opened, the wound was inspected, and a developing prolapse of the iris was immediately resected. The lids were closed, and a pressure bandage was applied for forty-eight hours. At the end of that time the anterior chamber was unformed, the lips of the incision were approximated, and one could see a dome-like elevation of the temporal half of the fundus. The patient was taken to the operating room, and, with use of local anesthesia, the conjunctiva was incised and a posterior sclerotomy made, with a cataract knife, below the level of the lower margin of the external rectus muscle, approximately 14 mm behind the limbus. A large amount of black, fluid blood was evacuated. Postoperative convalescence was interesting. The incision healed, the anterior chamber reformed, but throughout the rest of the period of hospitalization (approximately one month) there persisted a bilobed retinal detachment, situated temporally and toward the periphery, with one lobe above the other. The region of the macula remained free. The presence of a subchoroidal, or more likely an intrachoroidal, hemorrhage was undeniable. The sutures and the pressure dressing, with, perhaps, the quiet induced by the anesthesia, saved the eye from a catastrophic expulsive hemorrhage. With posterior sclerotomy this hemorrhage was evacuated satisfactorily. The recession of the choroid without simultaneous reattachment of the retina indicates a subretinal effusion of fluid from the vitreous, through the sclerotomy incision made in the retina. Enucleation was necessary one month later because of continued irritation and the development of photophobia in the opposite, normal eye.

In the process of disappearance of the hemorrhage, a picture appears which is similar to that shown in figure 7. Samuels, in discussing the histopathologic picture of expulsive and/or nonexpulsive subchoroidal hemorrhage and the manner of its disappearance, stated

phagocytes are rarely encountered, as is common in the periphery of blood clots in the vitreous and aqueous. Nor do the erythrocytes break up into granules. No shadow cells appear. As long as the hemorrhage is present, the red blood cells may show little or no change. They may persist for weeks. The exact mode of their disappearance is not clear. Probably they undergo chemical change, being dissolved, and in this way are carried off by the fluids of the tissues. As

<sup>11</sup> Samuels, B. Postoperative Nonexpulsive Subchoroidal Hemorrhage, *Arch Ophth* 6:840 (Dec.) 1931.



the quantity of blood diminishes, the capsule appears to contract or to collapse, so that when the lining finally coalesces merely a thickened membrane is left [fig 7]. In some preparations a row or two of cells indicate the line of union, and in other instances no sign of fusion is present. In the end, the suprachoroida is transformed over a greater or lesser extent into a thick, dense, avascular membrane free from pigment. Such thickening of the suprachoroida is often mistaken for the organization of an exudate after suprachoroiditis, when, as a matter of fact, it represents the collapsed capsule that once surrounded a hemorrhage.

Light is thrown on this matter in the examination of an eye enucleated four months after an injury. The suprachoroida was replaced over its entire extent, from the scleral roll anteriorly to the vicinity of the optic nerve, by a thick dense membrane [fig 7]. This lies like a ribbon in the sections, completely detached from the choroid and the sclera. Running along its center here and there are lymphocytes and some granules of blood pigment, marking the last vestiges of the hemorrhage.

There is little doubt that hemorrhagic detachment of the choroid is due, first, and most commonly, to rupture of the long posterior ciliary artery and, second, and perhaps rarely to rupture of one or more of the vortex veins. The first source applies almost universally to the operative opening of an eyeball, the second, perhaps most commonly, to traumatic perforation of an eyeball. In a third condition, trauma to an eyeball without perforation, hemorrhage may be from a vortex vein, from the long posterior ciliary vein, and, perhaps more rarely, from a choroidal artery or vein.

#### CHOROIDAL DETACHMENT FOLLOWING INTRA-OCULAR OPERATIONS (CLASS 2)

So-called choroidal detachment which follows intraocular operation is still, in the final analysis, of traumatic origin. In this type of detachment, however, as compared with that just discussed, intrachoroidal hemorrhage is rare, and the detachment is due almost entirely to edema or to an increase in transudation. Reuling<sup>12</sup> and Groenouw<sup>13</sup> and Meesmann<sup>14</sup> expressed similar opinions, long before Fuchs had stated his concept of the mechanism. Verhoeff<sup>15</sup> stated

he was not convinced, however, that the situation was so simple. He granted that the cause of detachment was the result of transudation of fluid from the choroidal vessels, as O'Brien stated, following opening of the eye and reduction of the intraocular pressure almost to zero, but he (Verhoeff) asserted that this fluid distended the perichoroidal space and compressed the vitreous. The persistence of the detachment, after healing of the wound, proved to him that fluid had been squeezed out of the vitreous by the displacement of the retina and the choroid.<sup>16</sup> This opinion seems to have clinical proof in the sequelae which appeared in some of the cases about to be presented. Certainly, with the resulting trauma to the choroid, the explanation accounts satisfactorily for the angioid streaks not uncommonly seen after detachment of the choroid.

Histologic study of such lesions is not as common as is their clinical observation. Many of them, as O'Brien has shown conclusively, run a fairly brief and uneventful course, others recede rather slowly. Less commonly, they have complications. Choroidal and suprachoroidal hemorrhage may accompany the choroidal edema. Atrophy of the choroid and retina may result, probably owing to the extensive damage to the choroid. The angioid streaks, when they appear, suggest that choroidal damage has occurred, also as Rycroft stated, if the anterior chamber remains uninformed for any great length of time, the danger of synechia in the anterior angle is serious.

Choroidal detachment following a cataract operation is not always a simple uneventful sequel of the surgical procedure. The following cases are illustrative.

CASE 5 (this case is but one of many similar, and uneventful, instances)—Mrs W., aged 64, had bilateral senile cataract. The state of the cardiovascular-renal system was satisfactory, and there was no hypertension or diabetes. A combined extraction was performed on

12 Reuling, G. Ablosung der Chorioidea in Folge von Cataract-Operation mit Glaskorperverlust, *Arch f Augenh* **1** (pt 2) 186, 1869-1870.

13 Groenouw, A. Zwei Falle von Aderhautablosung (scheinbarem Choroidealtumor) nach Cataractoperationen mit spontaner Heilung, *Arch f Augenh* **20** 69, 1889.

14 Meesmann, A. Experimentelle und anatomische Studien zur Frage der Aderhautabhebung, *Arch f Augenh* **90** 69, 1921.

15 Verhoeff, F. H. Scleral Puncture for Expulsive Subchoroidal Hemorrhage Following Sclerostomy. Scleral Puncture for Post-Operative Separation of the Choroid, *Ophth Rec* **24** 55, 1914, Pathogenesis of Glaucoma, *Arch Ophth* **54** 20, 1925, footnote 7.

16 Lindner, again in 1936, expressed the belief that this plasmod intraocular fluid, seeping through the vitreous, produced shrinkage of the vitreous by chemical action, and that this factor of shrinkage of the vitreous had much to do with choroidal detachment (Lindner, K. Zur Klinik des Glaskorpers die Zusammenziehung des Glaskorpers, *Arch f Ophth* **135** 332, 1936, Zur Klinik des Glaskorpers, die serose Aderhautabhebung nach Leckwerden des Augapfels, *ibid* **135** 462, 1936). Other investigators who might be mentioned are H. Knapp (Die intraocularen Geschwulste nach eigenen klinischen Beobachtungen und anatomischen Untersuchungen, Carlsruhe, C. F. Muller, 1868), Haab (Ueber Scheingeschwulste im Augeninneren, *Beitr z Augenh* **1** 103, 1891), C. D. Marshall (Detachment of the Choroid, *Ti Ophth Soc U Kingdom* **16** 98, 1895-1896), Velhagen (Ein Fall von Scheingeschwulste im Augeninneren nach Cataract-extraktion, *Centralbl f prakt Augenh* **21** 363, 1897), and Meller.



the right eye, without complications. One year later a similar operation was done on the left eye. On both occasions an intracapsular extraction was attempted but a capsulotomy extraction was done instead because of rupture of the capsule prior to the dislocation of the lens. The patient was discharged from the hospital twelve days after the operation, apparently without examination of the fundus. Two days later, at the time of her first visit to the office, one could see in the superior nasal quadrant, extending from the equator to the ora serrata, an area of so-called choroidal detachment. A notation of the lesion was made on the record, but the patient was not informed of the situation. Six days later the detachment had disappeared wholly, without any residuals. Vision with correction was 6/5 in each eye, with a normal-appearing fundus.

CASE 6—Mrs R., aged 52, was blind in the left eye, as a result of an old trauma. She was seen in consultation forty-eight hours after a corneoscleral trephination, performed because of simple, noninflammatory glaucoma. The pupil was semidilated, the anterior chamber unformed and the cornea clear. The entire temporal half of the retina bulged forward in a large gray dome, the apex of which seemed to be on a level with the plane of the pupillary aperture. The area of elevation lay close to the nerve head temporally and extended above and below it, resembling the horns of a crescent moon. The superior nasal portion of the retina appeared normal. The bulbar conjunctiva about the trephine flap was conspicuously edematous. The external rectus muscle was detached and the line of the ora serrata determined. A series of scleral punctures was made 4 mm behind the ora serrata, extending from the external edge of the superior rectus muscle to the external edge of the inferior rectus muscle, the line forming an almost complete half-circle. With the tip of a cataract knife, the scleral punctures were carried through the sclera. The puncture at about 10 o'clock showed a small amount of black, fluid blood, and at 7 o'clock a large quantity of black, fluid blood poured out through the sclerotomy opening. Additional punctures were therefore made behind this point, almost to the external limits of the insertion of the inferior oblique muscle. The external rectus muscle was reattached, and a pressure dressing was applied for forty-eight hours. Examination of the fundus at that time showed a notable recession in the elevation of the retina but no change in the area of involvement. One week later the level of the retina had become normal everywhere except for a grayish, shining dome in the neighborhood of termination of the long posterior ciliary artery. When the patient was seen one month later, one could see a large irregular half-ring of choroidal atrophy, which seemed to indicate the limits of the original choroidal lesion. No signs of the sclerotomy punctures were present. Vision was 6/9, and the field was full, no pathologic condition in the nerve head or in the peripheral nasal portion of the retina was visible.

One wonders whether the choroidal detachment in this case was due to rupture of the long posterior ciliary artery or to combined hemorrhage and transudation (see statement by Samuels, page 226). The immediate postoperative convalescence was uneventful. Two years later an intracapsular extraction was done for

subsequent formation of cataract. Subsequent examination of the fundus showed that the irregular ring of choroidal atrophy was still present as an irregular crescentic line of pigmentation, with contiguous areas of depigmentation. There must have been an acute folding of the choroid at this point.

Case 7 suggests that extensive and progressive choroidal atrophy was a complication of the postoperative situation.

CASE 7—Mrs M., aged 60, with bilateral simple, non-inflammatory glaucoma, had moderately severe hypertension and emotional instability. She had recently been widowed. There was apparently some renal damage. Vision was limited to mere light perception in the right eye, and was 6/60 in the left eye, with a cut in the inferior nasal field. The lens showed changes in the anterior cortex in both eyes, and the details of the fundus were barely visible in the left eye. The position of the nerve heads, which were just discernible, suggested glaucomatous cupping. No details of the fundus could be seen in the right eye, owing to the high degree of pathologic change in the cortex of the lens. Corneoscleral trephination, with complete iridectomy, was done on the left eye, without complications. No observations on the fundus could be made thereafter, but the early and marked immediate contraction of the nasal field above and below suggested either a high degree of choroidal detachment or immediate loss in the superior field following the operation for glaucoma, the result either of injury to the nerve bundle or damage to the retinal vessels. Within four weeks, however, the field widened to that present prior to operation. Continued impairment of vision due to progressive changes in the lens necessitated removal of the lens, six months later. An intracapsular extraction was done, without complication, section being made in the cornea, anterior to the limits of the filtering bleb at the site of trephination. A postoperative pathologic process was seen in the fundus, exactly similar to that in cases 6 and 9, that is, a yellowish red line of demarcation, irregular, but smoothly undulating from 1 to 5 o'clock—its most posterior portion a few millimeters behind the equator. The posterior edge of this line was sharply outlined, with fine granular pigment along each side, and between this and the ora serrata the appearance of the choroid suggested diffuse atrophy. The color in this region varied from pale red to gray, with fine clumps of pigment. The field of vision over an interval of three years has shown conspicuous progressive contraction, corresponding to this portion of the retina and the choroid. The macula is barely involved at present. Vision is 6/100, and with a telescopic lens it is 6/15. The ocular tension remains between 14 and 18 mm of mercury (Schiotz).

In case 8, one of intensely acute secondary glaucoma, apparently the result of a pathologic condition of the retinal vessels, the choroidal detachment was the most extensive in our experience.

CASE 8—Mr S., aged 50, a tailor, had always been in good health. A sudden attack of intensely severe, acute inflammatory glaucoma developed in the left eye. Moderate arterial hypertension had been present for some time. Forty-eight hours after his admission to

the hospital a basal iridectomy was done without complication and forty-eight hours later the fundus was examined because the patient complained of a continued high degree of visual impairment. The external results of operation were satisfactory. The preoperative tension of 80 mm of mercury had dropped to 54 mm prior to the iridectomy, and the tactile tension seemed normal at the time of the first examination of the fundus. The cornea was clear, but the anterior chamber was still somewhat shallow. With the ophthalmoscope, one could see two huge, portiere-like folds, which filled the entire medial and lateral portions of the vitreous chamber. Each fold had a sharp, precipitous edge, and the disk and the macula were obscured by these elevations. The superior retinal artery and the retina contiguous to it could not be seen. This is important in view of the subsequent observations in the case, but at this time the examiner was unaware of anything significant. Recession of the choroidal involvement was rapid. The first determination of the field of vision showed almost complete inferior altitudinal hemianopsia, the macula being barely spared. The field was not consistent with the fundic picture. Further recession of the choroidal edema revealed complete permanent occlusion of the superior temporal retinal artery, and it was assumed that this vascular situation was the cause of the sudden, intense acute glaucoma. The patient was kept under observation for two years. Because of a slow, but steady, elevation in ocular tension, a cyclodialysis was then done. Detachment did not again occur. The condition has now been quiescent for five years, the ocular tension at no time after the cyclodialysis being above 22 mm of mercury. The altitudinal hemianopsia has remained stationary. Certainly, the retinal vascular situation of itself did not play any role in the development of the hydrops of the choroid, but a general pathologic process of the arterioles, specifically, the preexisting disease of the choroidal vessels, may have been related to the detachment.

Case 9 is an interesting demonstration of choroidal detachment with grave hypotension, in which sequelae suggested the presence or development of bilateral mild, low grade uveitis. At no time could one surmise this from the appearance of the iris, the cornea or the anterior chamber. The late vascularization of the anterior capsule of the lens, the initial hypotension in the left eye, the rapid development of the complicating cataract and the inexplicable return of the glaucoma in the left eye seem to be more than interesting coincidences. We feel that uveitis may have a not inconsequential role in the production of so-called choroidal detachment. In this case, however, it is uncertain whether the uveitis preceded or followed the operation for glaucoma.

CASE 9—Dr W, aged 62, had bilateral simple, non-inflammatory glaucoma. The general physical condition was only fair. The patient was under the care of his general medical adviser because of vascular instability. Several episodes during the preceding year suggested early myocardial impairment. A corneoscleral trephination, with peripheral iridectomy, was done on the right eye, and ten days later a similar operation, equally uneventful, was performed on the left eye. Eight days

after the first operation examination of the fundus of the right eye showed a gray, elevated, smooth-domed area of so-called choroidal detachment, in the form of an inverted V. The nasal and temporal areas were of about equal extent, the involvement including a third of the peripheral temporal portion of the retina and slightly more of the nasal portions. Spontaneous and rapid recession occurred, without any permanent changes in the fundus. Recovery was almost complete at the time of the patient's discharge from the hospital.

Six days after the operation on the left eye the picture was similar to that in the right eye, but we do not know how long it had been present. The patient returned to his home ten days later. The so-called choroidal detachment on the left side remained unchanged for approximately six weeks. Rest in bed and dehydration had as little effect on its course as did the resumption of his normal physical activities.

In this case an external filtration blebs did not appear at the trephine opening until the choroidal detachment had receded. After recession of the detachment a large multiloculated filtering cicatrix developed. After recovery there was apparent in the fundus a faintly outlined, yellowish gray line of choroid streaks, one edge of which, forming the limit of the detachment, was sharply outlined. The other edge was indistinct and faded off imperceptibly into the remaining structures. The appearance was much like that of angioid streaks of the retina. There was little doubt that the detachment was choroidal, the result of a long-standing disturbance of the choroid. The lens of this (left) eye became rapidly cataractous. It was removed (by intracapsular extraction) through an incision in the inferior portion of the limbus, without any untoward event. This operation, which was performed one year after the corneoscleral trephining, was followed by a similar detachment of the choroid, though not as extensive and of only short duration. The glaucomatous condition returned shortly, even though the filtering bleb above was functioning. It had not been disturbed by the cataract extraction. Corneoscleral trephining was repeated at 6 o'clock on the limbus, without success. The eye is now sightless, though without pain, and tension is 60 mm of mercury (Schiotz). The lens of the right eye is now becoming cataractous, though vision is still 6/15. Recently, a fine network of superficial blood vessels has developed in the anterior capsule of the lens. The vascularization does not arise from the arteries of the iris. Dilatation of the pupil with eucatropine hydrochloride showed these vessels appearing on the anterior surface of the iris from the equator of the lens, presumably in the region of the ciliary body. The iris is normal, and there is no pathologic condition of the cornea. Ocular tension remains at 16 mm of mercury (Schiotz).

Case 10 suggests that detachment of the choroid may have a damaging effect on the lens through the development of low grade uveitis. Certainly, in the 2 cases presented (9 and 10) no signs of uveitis preceded the operation for glaucoma. The surgeon who operated on the left eye in case 10 assured us that there had been no uveitis prior to that operation. The first corneoscleral trephining was followed by failure of the anterior chamber to reform and by a huge choroidal detachment. The chamber did not form for over a month, and the detachment did

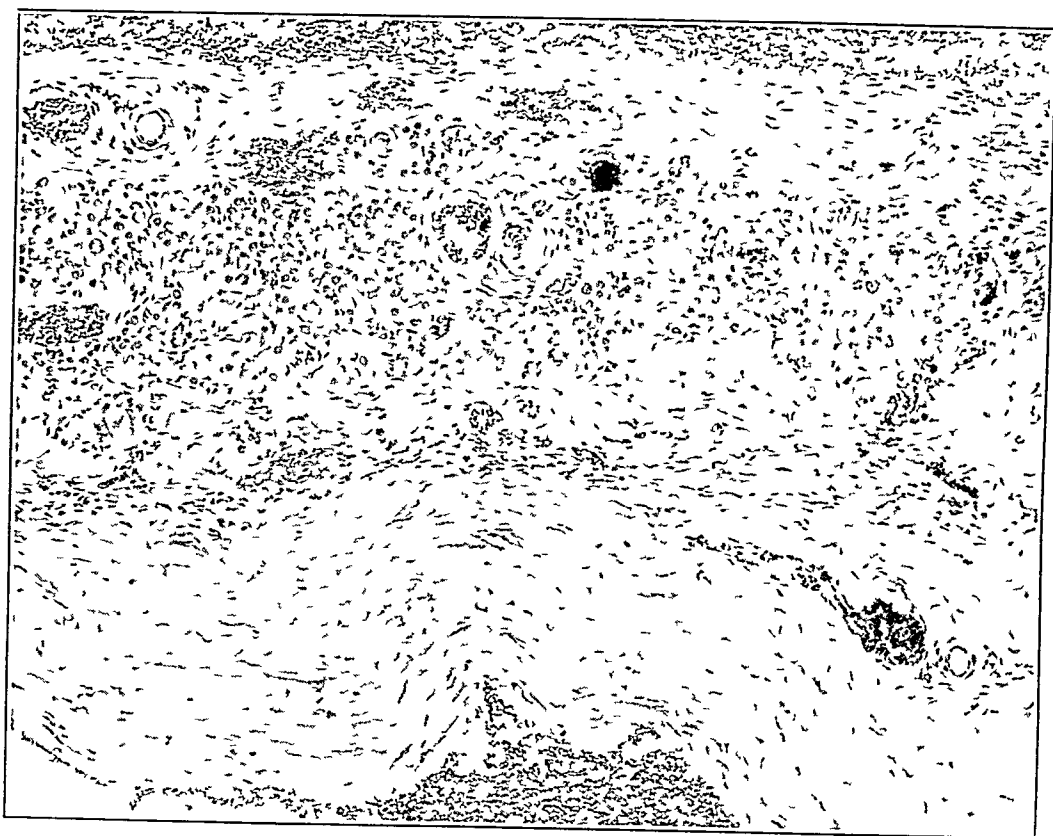


Fig 7—Late organization following exulsive hemorrhage

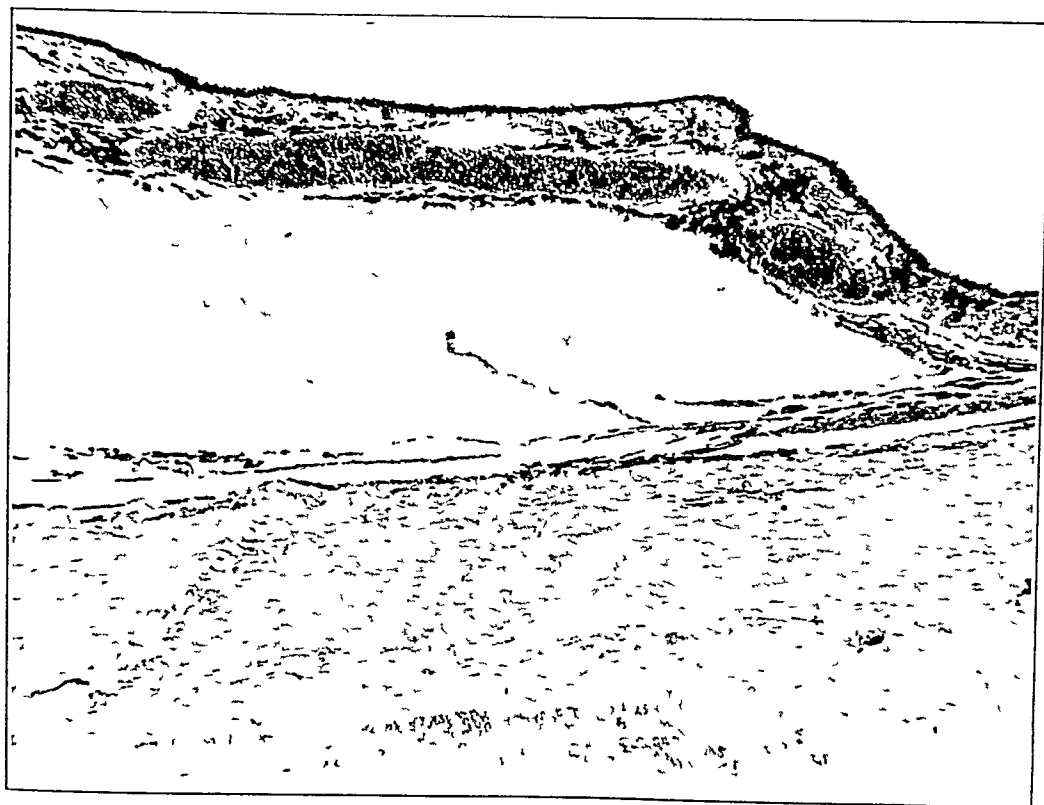


Fig 8—Choroidal edema following operation for glaucoma

not recede until after the anterior chamber had formed

CASE 10—Mrs McD, aged 60, was first seen one year after a corneoscleral trephination on the left eye had been done in another city for simple, noninflammatory glaucoma. Vision in the right eye was 6/6 partly, with the intraocular tension slightly below 30 mm of mercury (Schiotz). A corneoscleral trephining was done on the right side, with no complications. (The history of the immediate postoperative convalescence of the left eye was obtained from the surgeon.) Vision was slow in clearing after the second trephination, and the patient was hospitalized for almost a month. When she was first seen, less than a year after her first operation for glaucoma, the lens in the left eye showed a typical picture of developing complicating cataract. On the posterior surface of the lens was a diffuse quartzlike or

such a condition. The anterior chamber in the second eye to be trephined failed to reform for twenty-one days, though no hydrops of the choroid was evident.

The following 2 cases are interesting in that in each a choroidal and a retinal pathologic process were present.

CASE 11—F, aged 28, a linesman for an electric company, while sectioning a cable with a power wire cutter, was struck in the eye by a piece of the cable. On his admission to the hospital, he showed a laceration of the cornea just within the limbus at 1 o'clock, with a prolapse of the iris and a badly damaged lens. Roentgenographic localization showed a piece of steel wire, about 1 cm in length, lying in the vitreous chamber, between the equator and the ora serrata. A keratome incision

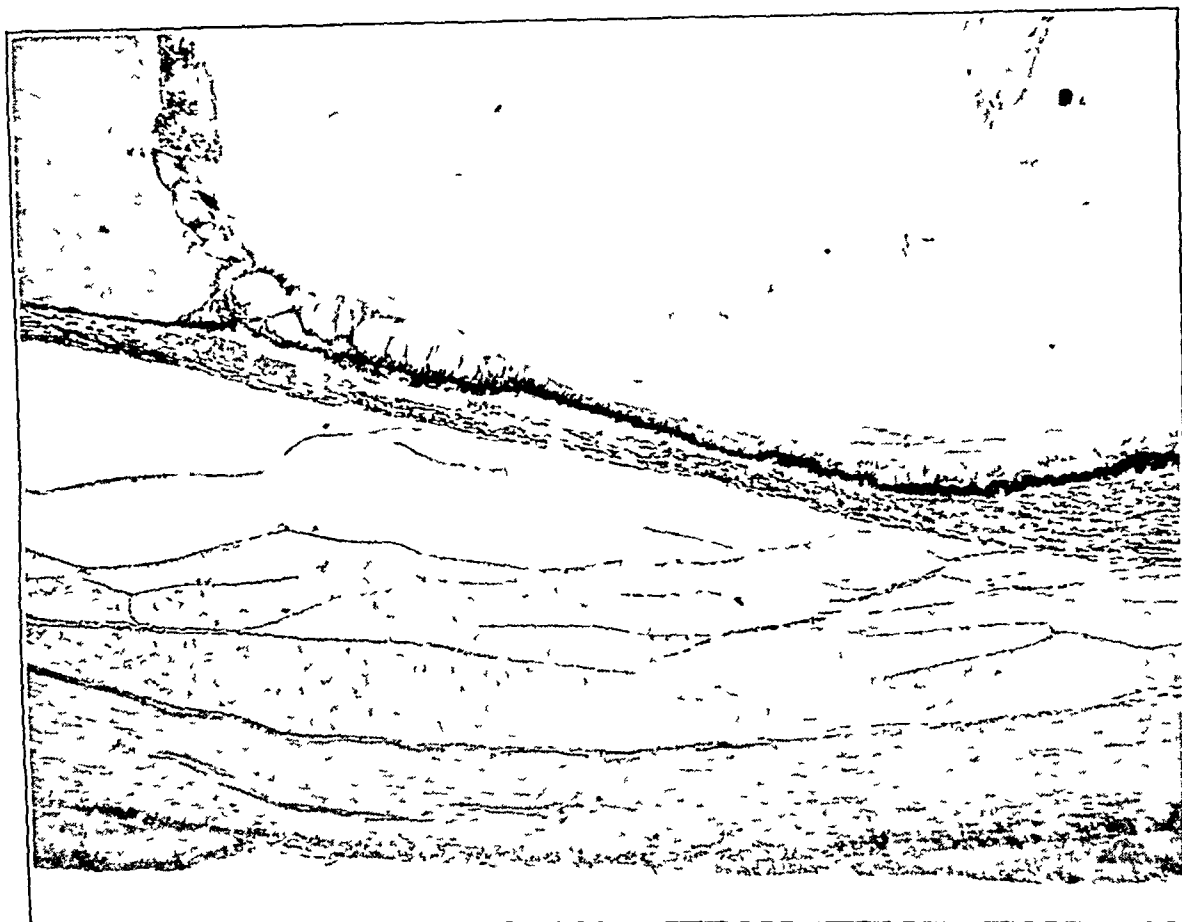


Fig 9—Perichoroidal detachment, with separation of the perichoroid, and subretinal transudates

limestone-like opacification, with a faint yellow tinge, and a similar opacity appeared at the periphery of the lens in the anterior subcapsular zone. There was a rapid and steady increase in the pathologic process in the lens. Vision is now less than 6/100, and the intraocular tension is between 10 and 20 mm of mercury. There is no lesion of the iris, cornea or anterior chamber. The field of vision is apparently normal. Examination of the right eye revealed no significant change in the lens. Measurement of the field of vision in this eye showed that recent involvement of the nasal fields had necessitated the operation for glaucoma. We can say with reasonable exactness that the first trephining was not accompanied by any surgical damage to the lens itself. The progress in the case, however, and the striking dissimilarity in the course of the disease in the two eyes are significant in support of our opinion that post-operative choroidal detachment at times may be accompanied by uveitis and at others may be the cause of

was made, the prolapsed area of the iris was resected, the fragments of the lens were washed from the wound, and the steel was extracted by a magnet, i. e., carried up across the surface of the iris and then removed from the anterior chamber. The operative wound was closed with a conjunctival flap. The patient made an uneventful recovery except for an area of detached choroid, which had receded wholly when he was discharged from the hospital, with the eye quiet. Vision at that time was 6/45 with a temporary, or trial, aphakia spectacle lens. Three months later the patient returned to the hospital with an area of retinal detachment overlying the former region of choroidal detachment. The sequence of events here is significant, in view of Rycroft's recent discussion. Now, however, one could see through the coloboma of the iris, even with oblique illumination, a linear rent in the anterior portion of the detachment, starting close to the ora serrata and extending across the equator, i. e., parallel with the antero-

posterior meridian of the eye. The original so-called choroidal detachment had been bulbous, firm and without movement of any kind, it was present at the time of the first dressing and receded slowly, but spontaneously. The retinal detachment was gibbous and

full. The choroidal detachment in this case was not due to subchoroidal hemorrhage. There was no choroidal or retinal laceration prior to the patient's first discharge from the hospital. Removal of the foreign body was by the anterior route, and the retinal separation was not

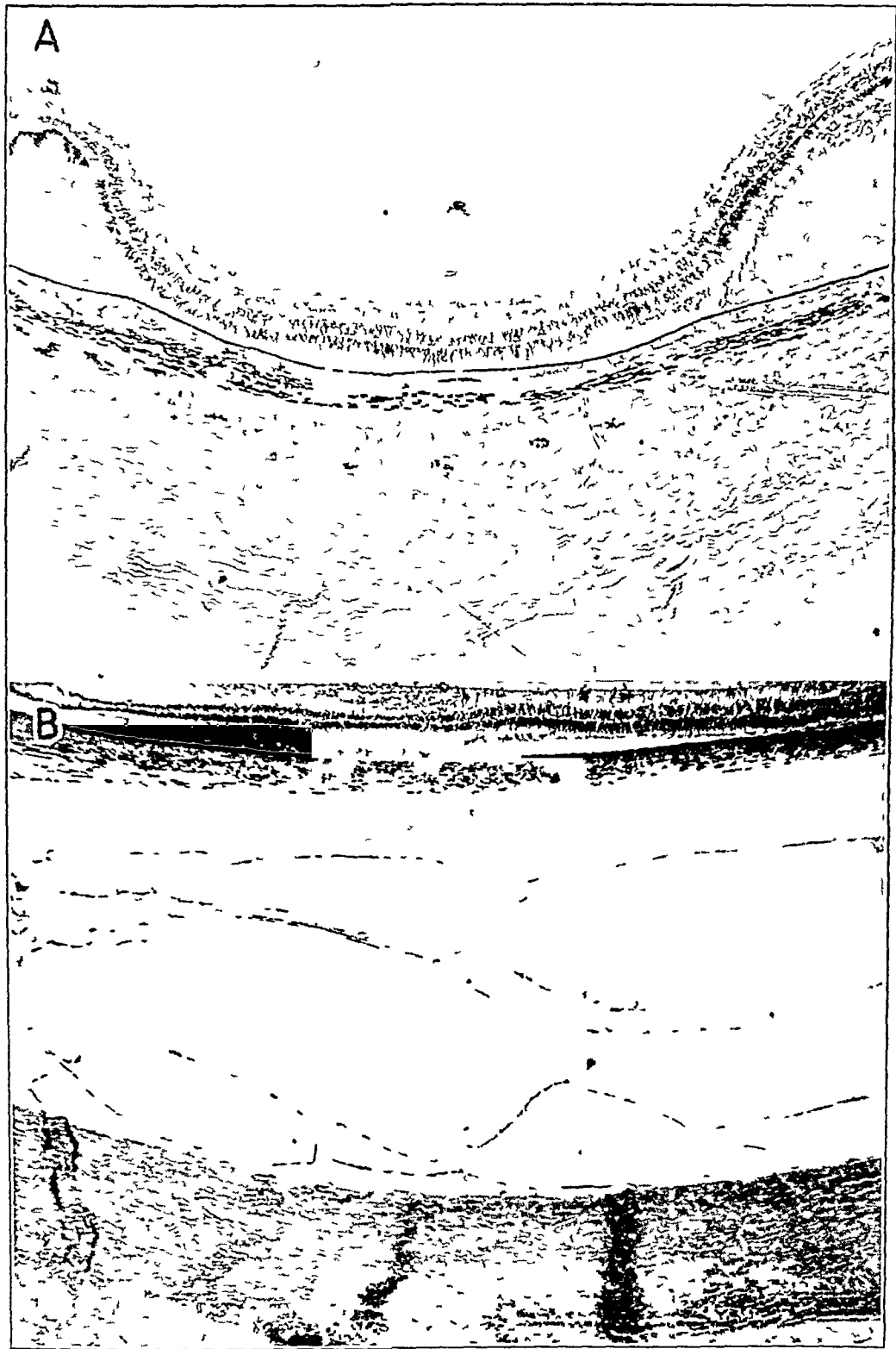


Fig 10—A, discrete subretinal transudates, B, portion of the area of choroidal detachment

flaccid, moved independently of and actively with the movements of the eyeball, had a demonstrable tear and responded to operation completely, with satisfactory results. Final vision three months later was 6/15 partly with the aphakia spectacle lens. The field of vision was

produced by sclerotomy. The choroidal detachment was the result of trauma and a surgical procedure, the retinal detachment may have occurred as a result of the choroiditis (uveitis) set up by the original damage to the choroid.

CASE 12—Mrs R, aged 62, had lost her right eye from an injury early in life. The left eye, when she was seen in consultation, showed an inferior choroidal detachment, which had appeared after an apparently uneventful recent corneoscleral trephining. The lens was mildly cataractous, and it was difficult to determine the exact condition present. Careful questioning of the patient failed to show whether the lesion was a true retinal detachment with glaucoma, whether it had been present prior to the trephining or whether it was a so-

examination of the fundus was made. In the region of the former choroidal detachment a similar situation appeared. At first glance, and without knowing the history in this case, one would have considered the diagnosis of choroidal detachment proper and plausible. Transillumination revealed impairment in the transmission of the light. The diagnosis, therefore, was that of an old, stationary retinal detachment, with perhaps an unrecognized neoplasm as the cause of the detachment. If not this, the findings on transillumination

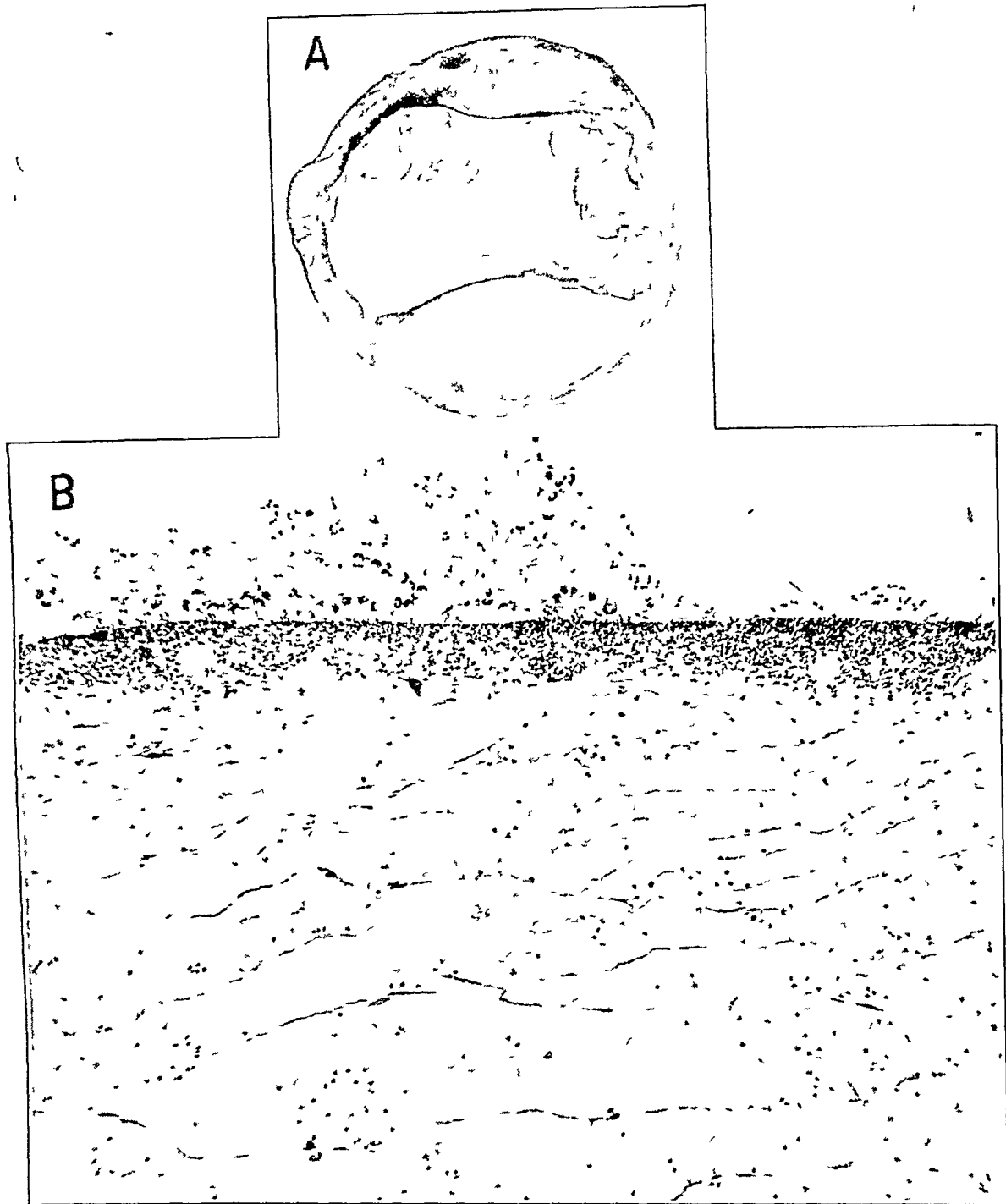


Fig 11—A, enucleation because of advancing suppurative uveitis following operation for secondary glaucoma B, portion of the area of choroidal detachment

called choroidal detachment. The weight of evidence seemed to favor the last. The attending ophthalmologist was advised to consider it as such and to keep the patient under observation. Six months later word was received that she had been admitted to the same hospital for extraction of a cataract. She was examined prior to this operation, but the details of the fundus were not visible. Determination of the field of vision revealed nothing significant. The patient had fair light perception and good light projection. Extraction of the lens was uneventful, and several days later a careful

would be difficult to explain. A retinal tear was not seen. Ten days or two weeks later transscleral diathermy punctures were made to determine the presence of fluid and to obtain a specimen for microscopic examination for the presence of tumor cells. The subretinal fluid did not flow freely, it was xanthochromic, somewhat viscous and of a sticky, stringy consistency. Microscopic diagnosis was negative for tumor. The condition was considered to be an unresolved subchoroidal hemorrhage (intrachoroidal and/or perichoroidal), dating from the first operation, with some organization

of a subretinal clot and with permanent, fibrosed, elevated, cystic degeneration of the choroid and the retina. The patient completely recovered after operation. She has a permanent defect in the upper part of the field of vision and for three years has worn without change a correction for 6/22 vision with her aphakia spectacle lens.

The histologic sections now to be described are from cases in which an intraocular operation was performed and histopathologic study revealed a choroidal detachment.

Figure 8 shows minimal deep hydrops of the choroid with coagulated serous fluid from the perichoroid which followed surgical intervention for glaucoma. There is considerable elevation of the superficial lamellas of the choroid from the deeper layers anteriorly. The eye was enucleated because of postoperative suppurating keratitis. The splitting of the choroid is evident at the edge

transudates. The appearance of the section suggests the possibility of traction on the choroid.

Figure 10A shows small areas of discrete subretinal infiltration close to the papilla, accompanied by minimal amounts of choroiditis. The areas of choroiditis were slightly offset from the subretinal pathologic process. In B an area of choroidal detachment lies between the region of the retinal separation and the ora serrata. The perichoroidal lamellas, which are fragmented, are thickened and separated from each other by edema. The minimal subretinal pathologic change is present also in this section. Chronic vascular changes of the retina and of the choroid are absent.

#### CHOROID DETACHMENT OF INFLAMMATORY ORIGIN (CLASS THREE)

The next histologic sections to be described are from cases of uveitis in which a pathologic

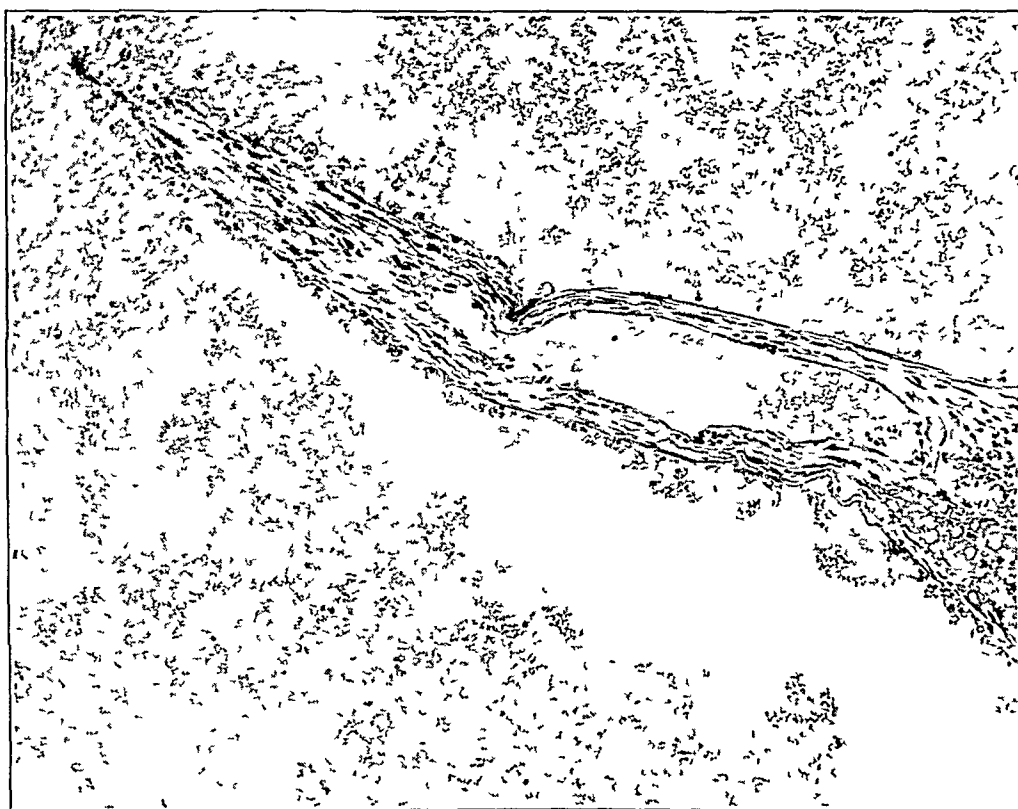


Fig. 12—High power magnification of an area of old uveitis with massive hydrops of the choroid

of the choroidal detachment. The eye was darkly pigmented, and because of this the splitting of the lamellas is more manifest. The choroidal vessels are engorged, with blood cells lying free in the choroidal stroma. The overlying retina was normal.

Figure 9 is a section taken after enucleation of the globe in a case of noncongestive glaucoma. The enucleation was done because of continued irritation following incarceration of the iris. (An iridencleisis had been done for glaucoma.) Preretinal hemorrhages lay free in the vitreous. A high degree of edema of the perichoroid extended to the ora serrata and beyond, into and beneath the ciliary body and continued posteriorly, past the equator of the eye. The choroid in places appeared normal. Cystic degeneration of the retina could be seen at the ora serrata. An area of retinal separation was also seen behind the ora serrata, with subretinal

condition of the choroid was observed microscopically. They have only one factor in common, inflammation, of a rather severe degree.

In only 1 case (fig. 11) had there been any surgical intervention, that apparently having been an operation for secondary glaucoma. The enucleation was done because of progressive suppurating anterior uveitis. The following figures demonstrate that inflammation is an important underlying factor in the causation of one type of choroidal detachment.

Figure 11 is from a case in which enucleation was done because of advancing suppurative uveitis following



operation for glaucoma *A* shows massive edema of the choroid in the upper and the lower part of the globe, with gross infiltration and destruction of the retina and exudates and hemorrhages into the vitreous. The edema of the uvea is evident. *B*, a section from the center of

with conspicuous subretinal exudates, infiltration and cellular debris. The exudate and hemorrhage into the vitreous are not shown, nor does the detachment shown include the sclera. There is little doubt that traction on the choroid may also have been a factor in this case.

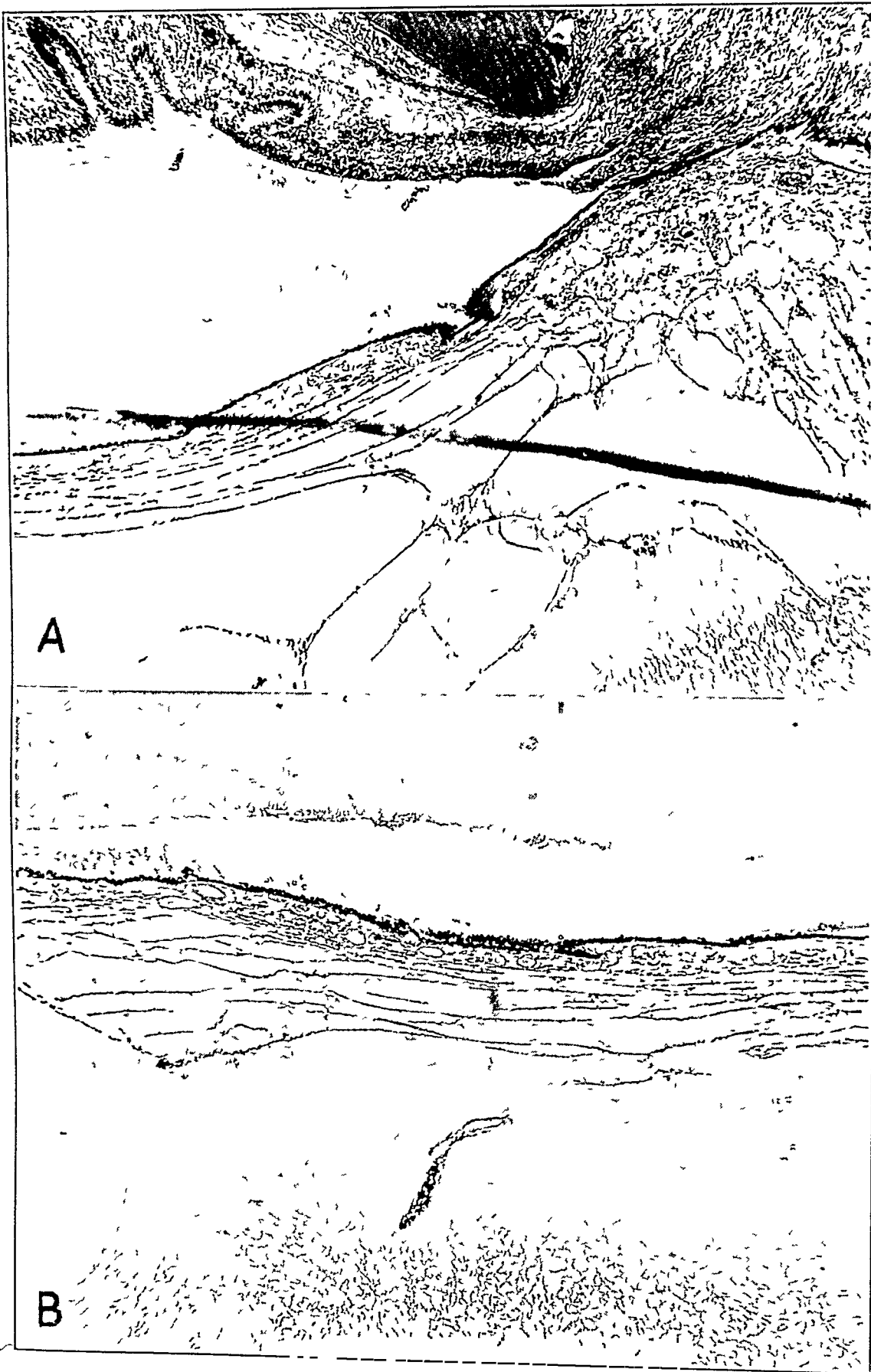


Fig 13—Detachment of the choroid due to traction

one of the areas of hydrops of the choroid, shows separation of the lamellae, with massive edema of the lamellae themselves. Areas of cellular infiltration lie along the lamellae. High power magnification revealed many clusters of polymorphonuclear cells. There are separation, contraction and degeneration of the retina,

The total cross section of the area of choroidal edema with the magnification shown was about three times the width of the photomicrograph.

Figure 12, from a case of long-standing uveitis with conspicuous massive hydrops of the choroid, is a high power study of the granular structure of the intra-



lamellar transudate (perichoroidal), with engorgement and infiltration of a choroidal vessel. The choroid was separated from the sclera by a subchoroidal serofibrinous exudate. A true retinal separation was present, with a

. In figure 13, from a case of uveitis, probably of long standing and undoubtedly of inflammatory origin, the anterior limits of the choroidal detachment are shown (A). There is massive edema of the perichoroidal



Fig 14—Generalized infiltration, with detachment of the choroid, the retina, the vitreous body and the anterior uveal tract.

stained transudate lying between the choroid and the retina, although the fluid was of a somewhat different consistency than that seen in the choroid itself or between the choroid and the sclera.

lamellas, especially in the deeper portions. The sclera, which lay below the section, is not included. This section shows a high degree of severity of an old pathologic process of the retina, with conspicuous retinal

separation. A portion of the degenerated, folded retina is included in the field (Figures 13 and 14 are excellent illustrations of choroidal detachment due to traction.) Subretinal hemorrhage, transudate and exudate are all present. A subretinal transudate, overlying the choroid, is readily seen in *B*. This section was taken at the highest point of the choroidal detachment, although it does not include the total cross section of the area of choroidal edema. The sclera in this section also lay near the bottom of the photomicrograph. Subretinal transudate lies at the top of the section. The edema of the choroid is well seen, as well as the deeper sero-fibrinous transudate.

Figure 14 *A* is taken from a case of plastic iridocyclitis with generalized infiltration and detachment of the choroid, the retina, the vitreous body and the anterior uveal tract. *B* is a higher magnification of a portion of the same field, showing separation of the choroid by an area of massive edema lying near the anterior peripheral portion of the choroid and passing into the ciliary body. The condition was pure inflammatory choroiditis.

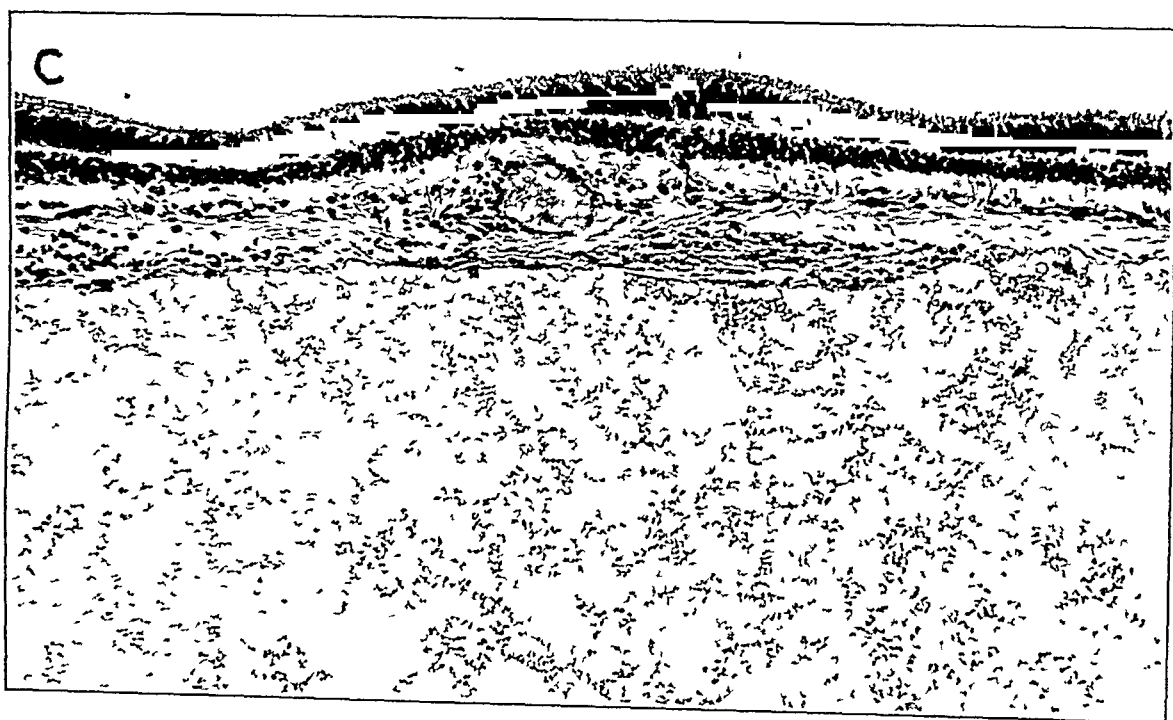


Fig 14 C—See legend on opposite page

*C* is from another site at the posterior pole of the same eye, showing further choroidal and retinal inflammatory changes, somewhat dissimilar but certainly chronic.

The sections in these cases of choroidal lesions of inflammatory origin illustrate edema, cellular infiltration, perichoroidal detachment and fragmentation with the formation of a lamellated appearance, due, probably and primarily in most cases, to the effect of traction of a contracting uveal tract, with the establishment thereafter of a vicious cycle. It is probable that in these severe lesions the process could never be reversible. The infectious process itself and the intraocular presence of the products of this infection may be responsible alone, in many instances, for a choroidal detachment, without the necessity of the development of any type of uveal traction, though only in the cases of more recent acute inflammatory conditions.

## SUMMARY AND CONCLUSIONS

On the basis of the clinical observations in the cases presented and, as a corollary, the study of the histologic sections, the following summary and conclusions are presented.

The term "choroidal detachment" is not essentially correct. So-called choroidal detachment may be due to massive edema of the choroid, a disturbance of the perichoroid or hemorrhagic choroiditis or a combination of the three conditions. It is doubtful whether an anatomic detachment of the choroid, that is, separation of the choroid from the sclera, occurs except as a result of trauma, either direct or postoperative, and then by dissection of the choroid from the sclera by a spreading, originally intrachoroidal, hemorrhage.

The term "massive perichoroidal edema" is a more correct designation for postoperative and post-traumatic conditions not essentially hemorrhagic.

That so-called postoperative choroidal detachment lies anterior, rather than posterior, to the equator of the globe is the result of the anatomic distribution of the choroidal circulation.

Traumatic postoperative and post-traumatic hemorrhagic choroiditis, also called subchoroidal hemorrhage, are frequently accompanied by massive edema of the choroid, and the two are to be considered as not essentially dissimilar. The first form includes the catastrophic expulsive (so-called subchoroidal) hemorrhage which not rarely follows intraocular surgical procedures.

So-called choroidal detachment, including surgical trauma, may have as an intangible partial cause a preexisting inflammatory condition, such

as low grade uveitis or a degenerative vascular situation. This is suggested in the postoperative changes in the lens in certain cases in which so-called choroidal detachment had occurred after operation for glaucoma. The choroidal streaks which remain, in some instances permanently, do not eliminate this possibility, neither do they confirm it.

Hydrops of the choroid is a frequent accompaniment of long-standing uveitis, as is seen histologically. The condition, while not different histologically from that following intraocular operation, is certainly the result of the uveitis or of the hypotony or of both, the one being consequent on the other.

With serious detachment of the choroid and the ciliary body, it has long been considered<sup>17</sup> (1) that detachment is the natural complement of a considerable reduction in the intraocular pressure, (2) that its occurrence is the rule in every case of sustained reduction of pressure, and (3) that the degree of the detachment varies more or less as the degree of reduction of intraocular pressure. While these statements are basically concurred in, the subject is not to be dismissed so conclusively. Hypotony is present, and it may be the cause of a detachment. The development in the choroid of an inflammatory process, or the extension of a preexisting one, subacute in some instances chronic in others, is, we think, a far more important factor. Many eyes with profound permanent hypotony were examined without there being an apparent increased incidence in choroidal edema or in perichoroidal detachment.

In cases of spontaneous, immediate, serous hydrops of the choroid following operation transscleral diathermy and drainage can be of no avail, by reason of the anatomic changes in the choroid. The condition recedes spontaneously without specific treatment. In cases of hemorrhagic choroidal detachment, immediate drainage through the sclera may be the means of saving the eye with useful vision. Choroidal detachment due to inflammatory changes is irreversible, and the prognosis is hopeless.

In the majority of instances immediate postoperative choroidal detachment should recede uneventfully with the closure of the operative wound or with closure of fistulas of choroidal or perichoroidal infiltration. Detachment appearing later after operation and detachment per-

sisting beyond the time of closure of the wound frequently cause considerable concern and may result in permanent damage to the choroid. Choroidal detachment which appears, in rare instances, very late after operation (Verhoeff and Waite<sup>18</sup> and Elschnig<sup>19</sup>) may well be the result of an undiagnosed pathologic condition of the uvea. Traumatic hemorrhagic detachment of the choroid is the result of more extensive damage to the blood sinuses than is a serous detachment or one due to free rupture of a long posterior ciliary artery, or even of a vortex vein.

To quote Dr Arnold Knapp,<sup>20</sup> in his differentiation of choroidal detachment as distinct conditions

serous and hemorrhagic subchoroidal detachment is a different clinical syndrome from choroidal changes which are so frequently observed in enucleated eyes, in which the lesion seems to be due to hypotony or to inflammatory changes.

While we concur in this statement, we believe that, regardless of cause, the entire process with the exception of traction of a diseased uveal tract (which is a late factor), arises from the blood vessels, in the form of edema transudates and pure hemorrhage, the transudation being from the choroidal veins into the perichoroidal space. To quote Duke-Elder:<sup>21</sup>

It is to be remembered that these veins, especially in the anterior region, are numerous and large, and are anatomically blood sinuses with a single endothelial wall.

A sudden release of external pressure will lead to engorgement, and transudation through their walls will be easy. Moreover, fluid withdrawn from beneath such a detachment is albuminous, containing fibrous, and some red corpuscles, and coagulates rapidly [O'Brien 1935], it is therefore derived from the blood and not the aqueous.

It seems, therefore, that as the source of the fluids is the same—subchoroidal, choroidal and perichoroidal—regardless of the immediate (or late) etiologic factors responsible for the so-called detachment the conditions are essentially similar pathologically, though differing in degree and in the end results.

1930 Chestnut Street

18 Verhoeff, F. H., and Waite, J. H. Separation of Choroid with Report of Spontaneous Case, *Tr. Am. Ophth. Soc.* **23**, 120, 1925.

19 Elschnig, H. H. Netzhautablosung im Anschluss an Chorioidealablosung, *Klin. Monatsbl. f. Augenh.* **86**, 595, 1931.

20 Knapp, A. Personal communication to the authors.

21 Duke-Elder, W. S. *Text-Book of Ophthalmology*, St. Louis, C. V. Mosby Company, 1941, vol. 3, p. 2540.

17 Collins, E. T., and Mayou, M. S. *Pathology and Bacteriology of the Eye*, ed. 2, Philadelphia, P. Blakiston's Son & Co., 1925.

# Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

## Cornea and Sclera

A NEW TYPE OF PIGMENT LINE IN THE CORNEA  
F W STOCKER and R E PRINDLE, Am  
J Ophth 27. 341 (April) 1944

Stocker and Prindle report a case of uveitis with a previously undescribed type of corneal pigment line. Eight months after the first examination there first appeared a fine line of brownish pigment, extending across the cornea from the limbus from 7 to 5 o'clock. A delicate branch with the same appearance radiated diagonally upward. The transverse line appeared to be a continuation of the limbal pigment onto the cornea. Biomicroscopic examination showed that the pigment line had a stippled appearance and was located in the most superficial layers of the cornea. Histologically, it lay within the epithelial cells of the cornea. Bowman's membrane was intact throughout, and both this membrane and the corneal stroma were free of pigment. The pigment did not take the iron stain and was considered to be melanin.

The article is illustrated W S REESE

TREATMENT OF HYPOPYON ULCERS WITH  
ALBUCID [SULFACETIMIDE] AND PRO-  
FLAVINE P D TREVOR-ROPER, Brit J  
Ophth 28. 181 (April) 1944

Twelve patients with hypopyon ulcers were treated with sodium sulfacetimide, 12 with proflavine and 1 by oral administration of sulfapyridine (as the last substance had an untoward effect, it was not tried again). Three patients with hypopyon iritis were placed under a regimen of irrigations with proflavine, and all rapidly responded.

For all but 4 patients no pathogenic bacteria were obtained in culture of material from the conjunctival sac, and for these 4 patients further culture after use of the bactericide gave negative results.

In 3 of each series of 12 patients, usually those with very old lesions, a Saemisch section was required. Those in the proflavine series were all over 60 years of age, and 2 octogenarians of the series treated with sulfacetimide lost the eye. All the 18 remaining patients had a history of pain for only a few days, in all the patients treated with proflavine the hypopyon cleared rapidly, in an average of two days, but in 6 of those treated with sulfacetimide, the hypopyon cleared in an average of five and three-tenths days, and in the remaining 3 patients it was still present on their transference to a base hospital after three, twenty-one and forty-two days respectively.

W ZENTMAYER

## Experimental Pathology

A STUDY OF EPITHELIAL REGENERATION IN  
THE LIVING EYE I MANN, Brit J Ophth  
28: 26 (Jan) 1944

Mann gives the following summary

"Sliding or migration of healing epithelium has been demonstrated in the living eyes of rabbits possessing a pigment ring in the conjunctiva at the limbus, and also in Nigerians who show the same condition.

"The slide can be produced by simple trauma or by chemical injury. It is not so easily produced by heat.

"The shape of the slide is determined by the shape and position of the epithelial loss and can occur onto the conjunctiva or the cornea equally.

"The rate and shape of the slide do not appear to be influenced by the nature of the injury nor the condition of the underlying substantia propria.

"The sliding of a pigmented limbus after trauma can be distinguished from pigment proliferation after chemical stimuli and from pigment migration without epithelial loss in vitamin A deficiency."

W ZENTMAYER

## Injuries

THE VALUE OF OPHTHALMIC TREATMENT IN  
THE FIELD G C DANSEY-BROWNING,  
Brit J Ophth 28: 87 (Feb) 1944

An analysis is made of 514 cases of ophthalmic injury from the Libyan campaign in which treatment was given at a mobile ophthalmic unit.

The types of wounds encountered and their treatment are outlined. In 14 of 67 cases of intraorbital foreign bodies treated the foreign body was extracted by the giant magnet at the base hospital. In only 1 case was extraction made in the forward area. In 22 cases the intraorbital foreign body had "perforated" the globe.

Owing to the terrain, about 200 men had to be operated on in the field unit.

It is suggested that "hospital infection" has been limited by local and oral administration of sulfonamide compounds, combined with a policy of "minimal interference" at the field medical units. No case of sympathetic ophthalmitis was reported in this series.

In 85 cases the wounds were of both eyes. In 45 cases the prognosis for the wounds of the two eyes was grave, and in 21 cases the men were subsequently reported as blind. Total disorganization of the globe occurred in 87 cases, and the eyes were removed at the mobile unit. In an

additional 27 cases the eyes were reported to have been removed at the base hospital

It is submitted that by general comparison with the statistics for the first world war the results obtained for this campaign have not been adverse

W ZENTMAYER

WAR SURGERY OF THE EYE AN ANALYSIS OF 102 CASES OF INTRA-OCULAR FOREIGN BODIES H B STALLARD Brit J Ophth 28: 105 (March) 1944

The patients were treated at a general hospital during the period from the offensive of General Cunningham's Eighth Army in the western desert, in November 1941, to the end of the North African campaign, in May 1943

In the analysis, the type of casualty, the nature of the missile, the site of penetration, the intra-ocular complications and the incidence of multiple wounds are noted. About 30 per cent of war missiles have low magnetic properties. When such a body is situated behind the lens, the posterior route of extraction through a scleral incision is the method of choice. The technic of this operation is described in detail.

Visual results and complications are discussed.

The article is illustrated W ZENTMAYER

A WASP STING S W K NORRIS, Brit J Ophth 28: 139 (March) 1944

A lance corporal complained of epiphora, pain and photophobia of the right eye. He had been receiving treatment for "keratoconjunctivitis." Vertical striae, which stained with fluorescein, were present over the upper third of the cornea. A small papule with a brownish center was seen in the middle of the conjunctiva of the upper lid. A fine hair was removed from the center of the papule. This proved to be "the distal part of the lancet of the sting of a wasp." It was then learned that about seven weeks before the patient had been stung on the right eyelid by a wasp.

W ZENTMAYER

### Neurology

A CASE OF ADIE'S SYNDROME T JAMES, Brit J Ophth 28: 190 (April) 1944

This pupillary anomaly was seen in a man aged 21, associated with absence of the right knee jerk, although a weak contraction of the quadriceps muscle could be detected, but only with reinforcement. The ankle jerk was absent on both sides. The superficial reflexes were normal. The triceps jerk on both sides and the knee jerk on the left side were normal. The Kahn test gave a negative reaction. The lens, fundus and tension were normal in both eyes. This case of Adie's syndrome did not present constantly all the features of the typical syndrome. At times the delayed "tonic" pupillary reaction was evident, and at other times it was not appar-

ent or was doubtful. The consistently smaller size of the right pupil and its strong tendency to maintain a constant diameter seem at first to indicate a parasympathetic tonus of the sphincter pupillae, the fact, however, that complete dilation of the pupil did not follow mydriasis with atropine suggests the contrary, a hypotonic state of the dilator pupillae. It is reasonable, therefore, to assume (1) that the relative smallness of the pupil was due also to relative hypertonicity of the sphincter pupillae over the dilator or (2) that, since the actual size of the pupil remained moderate, there was an almost atonic nerve balance.

It is submitted, therefore, that the delayed "tonic" pupillary reflex of Adie's syndrome is in reality "atonic" and is due to generalized nervous asthenia, the degree of which may vary from time to time, with a corresponding effect on the pupillary reflex, which is much more sensitive to such variations than are the sluggish tendon reflexes. Kyrieleis Werner's procedure appears to support this conclusion.

The benign and nonsyphilitic nature of the syndrome in a young and healthy person, who is capable of leading a normal life, is confirmed, and its detection appears to be a matter of chance. Its recognition, however, should become established among insurance company physicians, otherwise, the likelihood is great that a prospective policy will be refused because of the absence of reflexes, with the usual implication.

W ZENTMAYER

### Ocular Muscles

RECESSION OF THE INFERIOR-OBLIQUE MUSCLE FROM THE EXTERNAL-RECTUS APPROACH G P GUIBOR, Am J Ophth 27: 254 (March) 1944

Guibor describes a method of recession of the inferior oblique muscle by first exposing and temporarily tenotomizing the external rectus muscle. The latter is then reattached or otherwise dealt with, as indicated.

W S REESE

### Operations

TRANSSCLERAL LACRIMAL-CANALICULUS TRANSPLANTS G G GIBSON, Am J Ophth 27: 258 (March) 1944

This is a report on a series of experiments designed to lower tension by establishing an epithelial tube through the sclera. This work is still experimental and is not recommended as a clinical procedure, although one human eye was operated on with fair success.

W S REESE

A NOTE ON IRIDENCEISIS P J EVANS, Brit J Ophth 27: 548 (Dec) 1943

Iridenceisis, in common with all fistula operations, finds its best application in cases of non-

congestive glaucoma, either chronic or subacute. In cases of acute congestive glaucoma all manipulations of the iris or ciliary body are contraindicated if other procedures are possible.

Evans describes a modification of the operation of iridencleisis particularly applicable in cases of noncongestive glaucoma in which the iris is still elastic and the pupil still responsive to physostigmine. The scissors are applied, with the heel touching the globe and the points slightly raised, only about two thirds of the thickness (width) of the iris is cut, but the incision is carried to a sufficient length to provide a tongue which will easily reach the subconjunctival pouch through the lips of the incision. Replacement of the iris is effected by gentle external pressure over the corneal limbus and the temporal half of the wound, while a grip is retained on the tongue of the iris. By preference, the nasal pillar of the iris is included in the wound. Postoperative treatment consists of the use of massage and 0.5 per cent pilocarpine hydrochloride, with or without epinephrine. W ZENTMAYER

### Orbit, Eyeball and Accessory Sinuses

ORBITAL CELLULITIS IN A BABY CAUSED BY ACUTE OSTEOMYELITIS OF THE MAXILLA  
J A MAGNUS, Brit J Ophth 28:135 (March) 1944

A girl aged 2 weeks had had a cold with nasal discharge. There was proptosis of the eyeball with edema of the lids. Within two days the clinical picture was that of orbital cellulitis. On the fifth day after admission to the hospital an incision was made through the medial part of the left lower lid down to the bone. A large subperiosteal abscess of the floor of the orbit was opened, and excessive pus was discharged from the opening. A small fistula persisted, and about three months later a sequestrum, measuring 8 by 10 mm, was removed by forceps. The fistula then closed, and further progress was uneventful.

The article is illustrated. W ZENTMAYER

### Refraction and Accommodation

A NOTE ON THE SPHERICAL EQUIVALENT OF SPHERO-CYLINDRICAL LENSES  
W J RIDDLE, Brit J Ophth 27:302 (July) 1943

At a time when it is necessary to exercise simplicity in the prescription of glasses it may be of value to draw attention to a simple application of the principle of Sturms's conoid. The author cites Prangen's definition of the spherical equivalent of any formula for the correction of astigmatism as one equal to the value of the spherical lens plus half the value of the cylinder added algebraically. If the cylinder is reduced by any given amount, half of this should be added to the existing sphere. As the result of the war, the Council of British Ophthalmologists depre-

cates the prescribing of 0.125 D powers. For example, if this were done, an error in refraction corrected by  $+0.37$  D sph  $\subset -0.75$  D cyl, ax 180 would have no lens prescribed.

W ZENTMAYER

### Retina and Optic Nerve

COATS'S DISEASE  
J LAVAL, Am J Ophth 27:163 (Feb) 1944

Laval concludes that Coats's disease and circinate retinopathy depend primarily on changes in the arterial system of the retina, whereas senile and juvenile macular degeneration are the result of changes in the choriocapillaris.

W S REESE

A CASE OF EXUDATIVE AND HAEMORRHAGIC RETINITIS, WITH INCREASED INTRA-OCULAR TENSION, TREATED BY PILOCARPINE AND THYROID  
A LANDAU and J RUSZKOWSKI, Brit J Ophth 28:184 (April) 1944

A married woman aged 40, after a blow above the right eye, had retinal hemorrhages and, subsequently, an operation for glaucoma. Two years later the eye was blind. The globe was later removed. In 1942 hemorrhages and exudates appeared in the retina of the left eye. Later, glaucoma occurred, and vision was reduced to counting fingers at 18 inches (45.7 cm). Tension was controlled by use of pilocarpine. The cholesterol content of the blood was at the upper limit of normal, and the basal metabolic rate was  $-10$  per cent. In view of these findings, thyroid was given, and vision gradually improved to 6/18, fifteen months later the intraocular tension was maintained at a normal level, with use of pilocarpine.

W ZENTMAYER

### Vision

LESS EVIDENT CAUSES OF LOWERED ACUITY IN SENILITY  
R I LLOYD, Am J Ophth 27:232 (March) 1944

Lloyd discusses reduction of vision in older persons as caused mainly by corneal and macular disturbances and vascular accidents. He emphasizes the value of biomicroscopy and perimetry.

W S REESE

### Visual Tracts and Fields

THE PSYCHOGENIC COLOR FIELD  
J E REEDER, Jr, Am J Ophth 27:358 (April) 1944

In the neurasthenic patient there is a change in the way in which the colors are arranged and in the size of the field of colors. There is a notable decrease in the size of the form, as well as in the color. The fields are irregular in shape. The colors are interlaced, or they may be inverted. The colors may extend outside the form limits.

Reeder draws the following conclusions

"It has been demonstrated that the psychogenic color field is of definite aid in the establishment of a psychoneurotic diagnosis. It is tangible evidence in an otherwise abstract diagnosis. It is a test that cannot be faked, therefore malingerers cannot make use of it. As in all things medical, no claim is made that this test is infallible, but when the test is positive it is an aid to diagnosis. In this series all of the psychoneurotic patients did have the change in the color fields, from mild to severe. Eighty-seven cases were reviewed, 72 were separated from the service for psychogenic reasons, 19 of the 72 were discovered by their psychogenic type of color field before they had had any association with the neuropsychiatrist."

W S REESE

### Therapeutics

THE USE OF VASODILATORS IN ACUTE FUNDUS DISEASE F C CORDES, *Am J Ophth* 26 916 (Sept) 1943

Cordes cites cases of tobacco amblyopia, acute retrobulbar neuritis, optic neuritis, acute exudative choroiditis, chorioretinitis juxtapapillaris, acute closure of the central retinal artery, central angiospastic retinopathy and tuberculous choroiditis in which treatment was with the use of vasomotor dilators. The chief function of the therapy is to increase the supply of oxygen-containing blood to the anoxic capillaries and tissues.

If the lesion is of a serious nature, typhoid vaccine is injected intramuscularly in relatively small doses, followed as a rule by the subcutaneous injection of sodium nitrite. In the majority of cases sodium nitrite alone was used. The results were spectacular in most instances, owing in part to the fact that the patients were seen early and that they were in the relatively early age group. If the lesion has existed for a longer period, the prognosis is not good. Chronic lesions of the fundus in older patients who had considerable arteriosclerosis have not responded to vasodilator therapy.

W ZENTMAYER

HYPERPYREXIA IN THE TREATMENT OF ACUTE OCULAR INFLAMMATIONS H C KNIGHT, M EMORY and N CALLAHAN, *Am J Ophth* 27: 381 (April) 1944

Knight, Emory and Callahan reached the following conclusions:

"The results of pyretotherapy in the treatment of inflammatory diseases of the eye are excellent in many cases, offering the only means of saving partial or total vision.

"The most striking immediate result of treatment is relief of pain. The restoration of vision is slightly more delayed, but very remarkable in most cases, depending on three factors: (a)

the duration of the process before the start of fever therapy, (b) the number of treatments given while under the therapeutic regime, (c) the close cooperation of the ophthalmologist, first in persisting in the local treatment, and second in determining the point at which treatment is to be discontinued.

"It is evident that much vision may be saved by this method of therapy, and equally evident that it is not applied as much as possible even where it is available. It is desirable, therefore, that ophthalmologists become more aware of the usefulness of this therapeutic method, and ascertain the means at hand in their locality whereby they may make it rapidly available to selected patients."

W S REESE

### Toxic Amblyopia

A STUDY OF THE HISTOPATHOLOGICAL CHANGES IN THE RETINA AND LATE CHANGES IN THE VISUAL FIELD IN ACUTE METHYL ALCOHOL POISONING I S MCGREGOR, *Brit J Ophth* 27: 523 (Dec) 1943

In April 1942, 18 patients with poisoning from inhibition of methyl alcohol were treated in the Glasgow Western Infirmary. Seven were gravely ill and died in the hospital. The eyes of 4 of them, 3 women and 1 man, were secured for histologic study.

The author summarizes the histologic and clinical observations as follows:

The retina was examined in 4 cases with routine haemalum and eosin stains and by the method of examination in bulk after the tissue is stained with scarlet red and thereafter embedded and sectioned in gelatin. No changes in the ganglion cells of the retina could be attributed indubitably to acute methyl alcohol poisoning, either the lipid changes in the ganglion cells or the size and shape of the ganglion cells or the nuclear content.

The optic nerve in each case was examined in serial sections stained with hematoxylin and eosin, by Marchi's method and by a rapid staining method for myelin (Smith and Quigley), instead of by the Weigert-Pal technic. The optic nerves showed no abnormality. Four patients, who had been blind in the acute stage, were examined at the end of a year. One had no defect in vision, the second, a bilateral relative scotoma, the third, an absolute scotoma, with the other eye normal, and the fourth, a relative scotoma, with good vision in that eye and a normal fellow eye.

When death follows poisoning so soon, histologic evidences are few. The signs of acute poisoning are not sufficient to show whether the retinal tissue or the nerve tissue primarily succumbs. A review of the literature and the follow-up study of the cases described suggest that the poison acts on the center of the nerve.

W ZENTMAYER



# Society Transactions

EDITED BY DR W L BENEDICT

## COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

ALFRED COWAN, M D, *Chairman*

WARREN S REESE, M D, *Secretary*

Nov 18, 1943

### Diabetic Cataract: Report of a Case DR GEORGE J DUBLIN (by invitation)

Diabetic cataract is a distinct clinical entity. Rollo is to be credited with first speaking of cataract as a complication of diabetes. In general, this form of cataract may be of two types. The first is often observed in the adult in association with diabetes mellitus. It is similar in appearance to senile cataract, including the cuneiform, saucer-shaped and nuclear forms. Actually, there is no point of differentiation, and it is impossible to tell them apart by any known method of observation, even by slit lamp microscopy. In both senile cataract and the opacity of the lens in the adult associated with diabetes, microscopic examination with the slit lamp reveals vacuoles, fluid clefts and lamellar separation in the cortex, together with various opacities in the lens. Grandle in a series of 76 cases of diabetes noted changes in the lens in 41, with an average sugar content of the blood of 298.7 mg per hundred cubic centimeters.

The second type of opacity of the lens, the true diabetic cataract, occurs in diabetic persons under 35 years of age. It has been considered a rare condition. O'Brien, Molsbery and Allen (Diabetic Cataract, *J A M A* 103:892 [Sept 22] 1934) reported an incidence of diabetic cataract of 16 per cent in a series of patients under 35. In 1942 O'Brien and Allen (Ocular Changes in Young Diabetic Patients, *J A M A* 120:190 [Sept 19] 1942) reported another series of 260 cases of diabetes in persons under 21 years of age in which they found 36 cataracts (an incidence of 13.6 per cent). True diabetic cataract may assume one of three forms, but all have the same characteristic in that the opacities are subcapsular, immediately adjacent to the subcapsular line. The most common type is the snowflake cataract of O'Brien, which is subcapsular, whitish, irregular in form and size and truly resembles snowflakes. In the second type the opacities are arranged as irregular, large and small plaques, together with fine, dustlike, dirty brown opacities, which are subcapsular and strongly resemble the cuneiform senile cataract. The third, or malignant, type is

the bluish white opacity, in which the lens may become completely opaque and swollen in one to three weeks, "hydrops capsulae lentis." According to O'Brien and Allen, opacities of the lens in young diabetic patients occur invariably in persons whose diabetes has been poorly controlled or has been uncontrolled for several months. After stabilization of the diabetes, these opacities may progress slightly, but after six months of control they generally remain stationary.

The following case is presented.

#### REPORT OF CASE

Mrs M R, aged 22, white, was admitted to the metabolism department of Philadelphia General Hospital, in the service of Dr Anthony Sindoni. The patient had had diabetes for ten years, a sore throat developed six days prior to admission.

*Diagnosis*—The diagnosis was cervical adenitis and acute bronchitis. The chief finding of pertinence was the sugar level of the blood, which ranged from 245 mg, on the day of admission, to 356 mg per hundred cubic centimeters.

She had been receiving 60 units of insulin for uncontrolled and unstabilized diabetes. Routine ophthalmic examination showed normal external structures with normal eyegrounds, in both lenses irregular, dirty brown opacities, occurring as large and small plaques, involved the anterior and the posterior subcapsular zone. Some of these opacities were pointed, resembling the cuneiform type of senile cataract. There was a small clear area of cortex between the opacity and the subcapsular line. The remaining portion of the lens was entirely clear. Vision was 6/60, Snellen scale, in each eye, with correction it was 6/12 in each eye.

#### DISCUSSION

DR ALFRED COWAN O'Brien and his associates divide what they call diabetic cataracts into two types. The type that Dr Dublin reported resembles the senile disciform cataract. At first the opacity in the present case appeared to be just in front of the posterior capsule, but with the narrow slit beam it was seen to lie just behind the face of the adult nucleus, a narrow space being left behind the posterior capsule. The space was narrow because at the age of this patient, 22 years, the cortex is small. Usually opacities in the lens occur in the zone



of most recent development, but they lie deep, down to the last surface of discontinuity

In the case reported by Dr Dublin, the opacity was disciform, yellowish gray and similar in every respect to the ordinary senile type

DR JAMES S SHIPMAN I should like to come to Dr Dublin's defense, if he needs it. In my limited experience diabetic cataract has been rare

A patient under my observation for the past fifteen years has finally gone blind, not from cataract but from diabetic retinopathy, which was the first to appear in his case and was of gradual but definite progression. His blindness is due to the retinopathy, cataracts and superimposed secondary glaucoma. So diabetes takes its toll, and cataract is a complication, but whether it has a diabetic origin is hard for any one to say. I believe the criteria given by Dr Dublin are as good as any—namely, the age of the patient, the history of diabetes in the presence of a high sugar content of the blood and the position of the opacities outside the embryonic nucleus

DR H MAXWELL LANGDON Dr Dublin is accurate in saying that it is difficult to tell diabetic cataract from changes in the lens due to other causes. If a patient has cataract and a high sugar content of the blood with glycosuria, the cataract is usually said to be of diabetic origin, and probably it is, but I am doubtful whether the cause of the cataract is always the diabetes

In many cases cataract in young people is unexplained. I have 2 cases in mind, the first, that of a woman aged 26, with bilateral cataract, whom I have had under observation for over five years. She has been completely studied at Jefferson Hospital, with special reference to metabolic tests, definite signs of hyperthyroidism were found, and the thyroid was operated on. I have thought that interference with the parathyroid glands may have caused the lenticular changes. There was no sign of diabetes. The cataracts are gradually advancing, the vision of one eye being reduced to 2/60, and operation will undoubtedly be necessary

In the second case, a man aged 37 was visiting a patient of mine over the last fourth of July. After a slight accident, which had nothing to do with the eyes, he noticed that the vision of one eye was very defective. The following day I found that vision in this eye was limited to perception of light and that practically a mature cataract was present. The other eye was normal in all respects. He is a patient of Dr Harry Gradle, in Chicago, Dr Gradle examined him carefully one year ago and found nothing to indicate such a condition. If either of these patients had had diabetes, it would undoubtedly have been said that the cataract was of diabetic origin

There are many elderly persons with ordinary senile changes in the lens who have an increase in the blood sugar and some sugar in the urine. Such cataracts are usually classified as diabetic, and they may be, but it seems to me that it is open to question whether a better designation would not be cataract in a person with diabetes

In Dr Dublin's present case, the cataract undoubtedly is due to the diabetic condition

DR I S TASSMAN In line with what Dr Langdon has just said, it seems that other factors are involved in the occurrence of cataract in diabetic patients. The sugar concentration of the blood at any one time in such patients is probably not the determining factor in the production of cataract. One sees diabetic patients with a high level of sugar in the blood and no cataract or retinopathy. In other patients with a comparatively low blood sugar level, one may find cataract alone or in association with retinopathy. These metabolic disturbances do not affect all patients in the same way. When cataract develops in a young person with diabetes, it should be called diabetic cataract, but there are certain unknown factors present, in addition to the sugar concentration of the blood, which are probably causative in the production of the ocular condition

DR SOLOMON S BRAV About two years ago my son, Lieutenant S Brav, presented the case of a child, about 14 years of age, with diabetes. There was no pathologic process of the retina or diabetic retinopathy, but vision was reduced to about 2/200. The child was in school during the early course of the illness but could not make any progress, the question at the time was whether or not the ocular condition was congenital or diabetic. I think my son decided the cataract was of diabetic type. Personally, I could not differentiate between one form and the other

I operated on both eyes about a year ago, with resulting vision of 20/30 in each eye. The child, now about 16 years old, is doing well, the diabetes is still present, but there is no retinopathy

DR GEORGE J DUBLIN Differentiation of diabetic and congenital cataract in the young person should not present a great problem. The various layers of the lens develop at certain periods of life, and congenital opacities of these layers have a typical location and appearance. For instance, if a congenital opacity is limited to the embryonic layer, the opacity formed sometime during the first three months of uterine life. If the opacity is in the fetal nucleus, it occurred between the third and the eighth month of fetal life, and if it is in the infantile nucleus, it probably appeared during the first month after birth. The adult nucleus develops at about the age of 10 years or later, and an opacity of the corre-

sponding zone indicates involvement at the age of puberty

Congenital cataract, unless it is completely opaque, with obliteration of all layers of the lens, is comparatively easy to diagnose. A history of diabetes, with rapid onset, would be of great help in differentiation. It was previously mentioned that there is a malignant type of diabetic cataract called "hydrops capsulae lentis," a bluish white cataract, with pronounced edema. This, in my opinion, is the only type which may be confused with total congenital cataract. The other types of diabetic cataract progress slowly and do not mature within several weeks, as some authors have stated.

The diabetic cataract in the case presented here is about one year old. Examination of the eyes two years ago failed to reveal any opacity of the lens. O'Brien and Allen claimed that when diabetes has not been stabilized cataract is likely to develop. O'Brien stated that if six months or more elapses without good control, with poor control or without any control of the diabetes, the opacity is likely to develop; he further claimed that if the disease is under complete control or has been stabilized for approximately six months, the cataract rarely develops further. After the cataract reaches a certain stage, it remains stationary.

Diabetic cataract is similar to, and may be confused with, cataract associated with other endocrine disturbances, such as parathyroid disorders and tetany. In cataract associated with tetany the location is similar, the opacities being in the deep portion of the cortex, but frequently they are blue and green. Other glandular disturbances producing cataract are cretinism, myotonia atrophica and mongolism. The opacities associated with all these conditions are similar in location and appearance, and without a history and physical examination they are extremely difficult to differentiate from diabetic cataract.

**Epidemic Keratoconjunctivitis** DR H MAXWELL LANGDON, DR VAN M ELLIS and DR ROBERT D MULBERGER

Epidemic keratoconjunctivitis, first described by Hogan and Crawford (*Am J Ophth* 25: 1059 [Sept] 1942), is characterized by congestion and swelling of the conjunctiva and lids, at times a false membrane, more likely to be on the conjunctiva of the lower lid, frequent enlargement of the preauricular lymph glands, and round or ovoid dots on the cornea just below Bowman's membrane, which are highly refractile and may break down and show slight staining.

The disease in cases occurring in the eastern part of the country has not differed from this description. At times the cornea breaks down and takes a slight stain. In our experience, the course of the condition is irregular, and there is

no specific treatment, although we have not tried injection with convalescent blood. Many of our patients had a preexistent slight injury or inflammation of the eye a week to two weeks previously. Cultures show indifferent growth, usually diphtheroids or *Staphylococcus albus*.

Murray Sanders (Epidemic Keratoconjunctivitis ["Shipyard Conjunctivitis"] I Isolation of a Virus, *ARCH OPHTH* 28: 581 [Oct] 1942), reported the isolation of a virus which produced encephalitis in mice and, after injection into a healthy man, who acted as a volunteer, produced conjunctivitis, although the author did not mention corneal complications.

The corneal dots may entirely disappear or may leave faint gray areas behind them. All our patients had complete recovery of vision to normal or better, although in 1 patient it was reduced to as low as 5/30 during the acute phase. In none of our patients could we trace any definite connection with an infected patient. We regard the corneal dots as the most definite diagnostic sign.

Our treatment consisted mainly of use of boric acid and phenacaine hydrochloride for relief of the discomfort, ice compresses for the swelling, tannic acid or silver nitrate for the catarrh of the conjunctiva, and, in the later stages, boric acid ointment U S P for massage, which we feel aided in the clearing of the cornea.

We had 45 patients with corneal complications—31 males and 14 females, both eyes were involved in 7 patients, the right eye in 23 patients and the left eye in 15 patients.

In some of our cases of most severe involvement the disease was binocular, which makes us feel that these patients were particularly susceptible. We have had about 25 other patients with what we feel was the conjunctival form of the disease, but they did not have corneal complications.

DR EDMUND B SPAETH. Dr Alton E Braley, in Chicago at the recent meeting of the American Academy of Ophthalmology and Otolaryngology, presented an analysis of some 300 cases of this form of keratoconjunctivitis. He emphasized something which neither Dr Langdon nor I had seen before, i e, recurrence, when patients with this disease recover they usually remain well. Also, their symptoms may disappear while they still have clinical signs of disease of the infiltrated cornea. For that reason, the case of the young woman which I shall present here is interesting.

The patient consulted me ten weeks ago with severe unilateral keratoconjunctivitis of the epidemic type. The condition was so severe that she had to be hospitalized. Ten days later she was out of the hospital, and ten days afterward she was back at work. Six weeks later she returned, with the lids of the right eye swollen, due to edema, and with lacrimation, photophobia and a sticky discharge. This was

not a recurrence because she had not recovered though she had apparently recovered clinically, now, six weeks later, she has almost as severe symptoms as she had at the first attack

With regard to treatment, and I speak personally, because I had the condition, Dr Langdon's statements about therapy are correct. The best treatment for the disease is early application of cold compresses to the eye, and later heat, a bit of epinephrine and enough pentacaine to keep the patient comfortable. Sulfathiazole was of no value whatever. As a matter of fact, it seems to irritate the eye. The therapy in my own case was suggested to Dr Shipman and me by another physician, Dr Kennedy, who had had the condition earlier, and who had gone through the same useless round of therapy. It is now known that specific serum, if administered early in the condition, relieves the symptoms to a notable degree and apparently shortens the course of the disease.

DR A G FEWELL During the epidemic of keratoconjunctivitis this spring I saw about 12 cases. My experience was the same as that of Dr Langdon in that no 2 cases were in the same family. My cases were from all sections, some from outside the state, and in all the glands were involved.

None of my patients had mucopurulent discharge, although there was considerable tearing, with some ropy secretion. The majority of my patients had bilateral involvement and all but 1 had some infiltration of the cornea. The patient who had no involvement of the cornea was the only one who was given convalescent serum, and the infiltration cleared up in a week. The other patients were treated with pentacaine and epinephrine, and with a few I tried a sulfonamide compound but none of these measures seemed to shorten the course of the disease. The majority of the corneal lesions were treated with Pregl's solution (containing the sodium salts of hydriodic acid and iodic acid with iodine [0.04 per cent]), which seemed to help the opacities clear a little more rapidly than those for which it was not used. In most of my cases the condition lasted from four to five weeks.

DR AARON S BRAY I have seen many patients with this disease. Most patients have chemosis, and a notable symptom is severe burning of the eye. I have not seen any patients with mucopurulent discharge. I have seen 2 patients with what looked like a pronounced membrane on the lower lid. Physicians say that they have never seen a distribution of the infection in a family. On the contrary, I have 6 patients in one family, and I am still treating them. A grandmother and child were in my office yesterday.

As for the mucopurulent discharge, I should say that was due to a mixed infection. As for the transmission of the disease, 1 of my patients

complained to her physician that she was sure she got the infection in my office. She had consulted me for refraction, and about two weeks later the severe burning sensation appeared. There were several patients with the conjunctivitis in my office at that time. In St. Louis they think that the mode of transmission is through the physician's office.

I am not as lucky as Dr Langdon. In my cases the corneal opacities did not clear completely. In fact, my daughter has had the disease nearly three months and still has numerous, probably ten to fifteen, centrally located opacities in the cornea, and her vision is reduced to 20/30 +.

As to treatment, I have had the same discouraging results.

DR IRVING L PAVLO At Wills Hospital we residents have seen several hundred patients with this condition during the past year. A number of factors indicate that it is infectious. Several waves of infection have occurred among clinic patients with glaucoma who had determinations of tension at short intervals with the same tonometer, which must have been insufficiently sterilized. Also, in the wards for patients with cataract, there have been several severe waves of infection, twice necessitating a quarantine of those wards. Most of the epidemiologic evidence points to an incubation period of eight to eleven days, more often the latter. This was shortened in the case of patients infected after cataract extractions, many of whom showed the fully developed disease by the time of the second or third postoperative dressing. It is interesting to note that none of these patients had any intraocular complications. The wife of one of the three resident surgeons who were victims of the condition had the disease after a clearcut incubation period of ten days.

DR ALFRED COWAN The incidence of epidemic keratoconjunctivitis among ophthalmologists is rather high. I have seen 3 well known ophthalmologists with the disease.

DR H MAXWELL LANGDON As for patients getting it at the physician's office, most of our patients picked it up on their own account. Boric acid ointment massaged daily on the eye, with a little placed under the lid, clears the opacities of the cornea better than anything else that we have tried.

#### External Ophthalmoplegia DR VAN M ELLIS

A Negro girl was first seen at the Presbyterian Hospital clinic at the age of 1½ years, at which time the mother stated that both eyelids had been drooping for the past two weeks. She has been under observation in the clinic up to the present.

The condition at present is as follows:

Vision is 6/30 in the right eye and 6/12 in the left eye with correction. The pupils are

equal and react to light and in accommodation. The patient has ptosis and complete palsies of the third, fourth and sixth nerves, the eyes are immobile, the right eye diverging about 20 degrees. The internal structures of both eyes are normal.

The child has been studied in the pediatric, neurologic, orthopedic, rhinolaryngologic and dental clinics. The neurologic condition, except for the ocular condition already described, is normal. The pediatricians consulted suggested that the child's ocular condition was the result of congenital syphilis, however, repeated Wassermann tests have all given negative reactions. Palpable epitrochlear glands are present. There is, however, a family history of syphilis, inasmuch as the mother and the younger sister are now under treatment at the Graduate Hospital.

Myasthenia gravis has been ruled out by therapeutic tests with physostigmine and electrical reaction tests. The rhinolaryngologic examination gave negative results. Roentgenographic examination of the skull and the sinuses revealed nothing unusual. All laboratory examinations, including studies of the spinal fluid, gave normal results.

Hence, the case is one of external ophthalmoplegia, the cause of which at present is undetermined.

DR GEORGE F J KELLY: Did Dr Ellis say this condition started a year and a half ago?

DR VAN M ELLIS: At the age of 1½ years.

DR GEORGE F J KELLY: It is not likely that the condition is congenital ophthalmoplegia if it came on at the age of 1½ years.

**Exudative Choroiditis** DR I L PAVLO (by invitation)

A man aged 26 entered Dr Fry's ward service at Wills Hospital on Nov 3, 1943 with vision in the right eye of ¼/60. The loss of vision had occurred three weeks previously, or ten weeks after onset of an atypical pneumonia, which had left a residuum of hoarseness and persistent cough, with much tenacious, nonfoul, mucopurulent, blood-tinged sputum. Visual difficulties began after a night of severe coughing.

Examination of the right eye showed small gray keratic precipitates, aqueous flare, mydriasis, clear lens, slight haziness of the vitreous, a light yellow-gray area of exudate, measuring 2.5 disk diameters, over the macula and disk, elevation of the disk of 2 D, with small hemorrhages, dilatation of veins and perivasculitis.

The visual field for 10/1,000 showed a cecentral scotoma, measuring 34 by 43 cm. The left eye was entirely normal, with 6/6 vision.

Two carious teeth were extracted. Drainage of a maxillary sinus, which was acutely infected, yielded frank pus, which, unfortunately, was not examined bacteriologically. Ten days later the sinuses were clear.

There were rales at the base of the left lung. A roentgenogram showed homogeneous haziness over the lower lobe of the left lung, with faint mottling; this was thought not to be tuberculous. The heart and blood pressure were normal. The possibility was considered that the pulmonary condition was typical chronic pneumonia due to *Bacillus Friedlander*. *B. Friedlander* was observed in pure culture in the sputum, which contained no acid-fast organisms. Successive cultures of specimens of the sputum yielded mixed growth, with progressively fewer *Friedlander* bacilli; typing was not done. Smears of prostatic secretion contained no gram-negative diplococci. Urinalysis, serologic studies, determinations of the blood sugar and sedimentation time and agglutination tests for brucellosis revealed nothing abnormal. Studies of the blood gave normal results except for leukopenia, the white cell count being 4,500 per cubic millimeter. Intracutaneous injection of 0.0002 mg of purified protein derivative produced a 2 plus reaction for tuberculin.

The patient had a subfebrile temperature, which gradually fell to a normal level. His cough slowly cleared. The exudative choroiditis showed progression in extent and severity, at one point suggesting early proliferative retinitis.

The morphologic, cultural, manifold pathologic and serologic properties of the *Friedlander* bacillus, or *Bacillus mucosus capsulatus*, are discussed. The unusual, chronic type of pneumonia caused by this organism is consistent with the clinical picture presented by the patient. Persons in the younger age groups have a definite resistance to the organism.

Investigation of the pathogenesis of uveitis rarely gives evidence susceptible of scientific proof, as attested to by Berens and associates in their negative cultures of the blood, aqueous and pharyngeal secretions for the causative organism in 91 patients with this disease. Morphologic or cultural proof of actual invasion of the uvea by an organism is rare, as is evidence of direct irritation by bacterial endotoxins or exotoxins. Hypersensitivity to allergens produced by bacterial foci rests chiefly on evidence of a clinical nature and admits of wide divergence of opinion as to the relative importance of pyogenic foci and of tuberculosis and syphilis.

In summary, this patient with exudative choroiditis presented an unusual variety of possible etiologic factors, including pulmonary infection due to *Friedlander's* bacillus.

DR W E FRY: My associates and I examined carefully every patient with acute "exudative choroiditis" at the hospital, and it has been our experience, and probably that of others, that in a number of cases we do not find, or are not sure of, the cause of the ocular difficulty. Dr Pavlo's case illustrates just the reverse situation. So many causes are suggested that one can take one's pick.

This patient will present an interesting problem. If one should examine him several months from now, at which time his pulmonary condition will probably have entirely cleared and any other focus of infection secondary to the pulmonary condition have disappeared, and should find a positive tuberculin reaction, one might conclude that the patient had tuberculous choroiditis, whereas the present evidence suggests that the real cause is a pulmonary complication.

#### Epibulbar Tumor Report of a Case DR W E FRY

A woman, in April 1915, at the age of 34, first noted a small pigmented lesion at the limbus of her left eye, at 1 o'clock. In October 1916 the lesion measured 4.5 by 2.5 mm and extended 1.5 mm into the cornea. The patient was first under the observation of Dr. Holloway and more recently under my care. April 1941 the eye was enucleated. The patient is at present alive and well. The nodule was excised in January 1920, and the pathologic diagnosis, made by Dr. Case, was that of melanosaarcoma. A nodule was excised a second time, and three applications of the thermophore were given. The lesion recurred locally and traveled about the limbus in a counterclockwise direction. There has been no evidence of metastasis.

*Pathologic Report of the Enucleated Eye*—Section of the eye revealed a deeply pigmented tumor near the periphery of the cornea. The mass in the section measured 3 mm. It was composed of pigmented, elongated and spindle cells. The nuclei were deeply stained and varied moderately in size. The associated inflammatory reaction was evidenced by clusters of polymorphonuclear cells. The mass was entirely superficial to Bowman's membrane. The tumor was partly divided by a band of dense connective tissue. All the superficial portion of the cornea was involved by tumor cells to a varied degree. These were seen at places within, as well as below, the epithelium and beneath superficial bands of connective tissue. A band of partly hyalinized connective tissue spread across the

cornea above Bowman's membrane. Bowman's membrane was unbroken, and the stroma beneath the membrane appeared normal.

The remaining portions of the eye were uninvolved except for an unusual number of pigment granules in the corneal trabeculae.

*Conclusion*—Certain portions of this report may be emphasized. The patient has been under observation twenty-eight years. The tumor was of a type usually considered highly malignant—melanosaarcoma. In spite of recurrences, the final pathologic examination revealed that the corneal involvement was entirely superficial. There has been no distant metastasis—if there had been, the patient would have died years ago. The tumor apparently possessed only the property of local recurrence.

An additional point of interest is that, although microscopically the cornea appeared remarkably clear, visual acuity was less than 6/60. This is of importance in the correlation of experimental corneal disease and the effective result of treatment.

DR JAMES S SHIPMAN Why was radium not employed in this case, and what might have been the result if it had been used? In most of the cases at Wills Hospital, Dr. Widmann advises irradiation before excision, and my associates and I have followed that policy routinely with epibulbar growths. After excision, a correct diagnosis can be made, and further irradiation can be carried out if indicated.

Dr. Fry stated that Colonel Ash expressed the belief that irradiation was unnecessary for carcinoma. Why is that true, and does the same thing hold for melanosaarcoma?

DR W E FRY This patient was seen on at least one occasion, perhaps on several, at the roentgenographic department of the university, and irradiation was advised against.

Dr. Shipman is in agreement with some persons with regard to irradiation. For instance, Dr. Reese, in a recent discussion of the treatment of precancerous melanosis of the conjunctiva (*Tr Am Acad Ophth* 47:420 [May-June] 1943), recommended excision and irradiation by application of radon directly to the site of the growth.

## Correspondence

### VERNAL CONJUNCTIVITIS

*To the Editor* —In a letter published in the June issue (ARCH OPHTH 31:557, 1944), Dr Louis Lehrfeld, of Philadelphia, severely criticizes my article entitled "Ariboflavinosis as a Probable Cause of Vernal Conjunctivitis," which appeared in the March issue (ARCH OPHTH 31:214, 1944). I am making the following comments, not for the purpose of starting a fruitless discussion, but in the hope that they may clarify some of the points brought out in Dr Lehrfeld's letter.

First, I wish to point out to Dr Lehrfeld that my theory neither attacks nor excludes the theory that in certain cases vernal conjunctivitis may be an ocular manifestation of an allergic state. However, it would be difficult to prove that every case of this disease has an allergic condition as its only cause. In my article, I merely suggested that ariboflavinosis may be one, not necessarily the only, cause of vernal conjunctivitis.

Dr Lehrfeld states that he disagrees with my theory, which "lacks scientific confirmation." This is necessarily true, as sufficient time has not elapsed to allow other authors to prove or disprove it, in the latter case I should be the first to admit the facts. He also expresses surprise that I did not mention vernal conjunctivitis as an ocular manifestation of an allergic state, and he continues by citing facts in support of the allergic theory. Later, he states that the description I gave of the disease differs from descriptions he had already published (Lehrfeld, L. Observations on Eighty-Seven Cases at the Wills Hospital, ARCH OPHTH 8:389 [Sept] 1932; Lehrfeld, L., and Miller, J. Additional Research on Vernal Conjunctivitis, *ibid* 21:639 [April] 1939).

On the first page of my article, second column, line 17, I stated "Other authors have attributed it to various conditions such as hay fever and anaphylaxis, generally the cause is stated to be unknown." I did not consider it necessary to enter into more detail concerning all the etiologic theories of vernal conjunctivitis or to give a more elaborate description of the illness, as my primary purpose was to set forth the theory of the role of riboflavin deficiency on the basis of the results obtained with this vitamin, leaving to others more capable than I the minute pathologic description of the disease.

It appears that not all authors admit allergy as the cause of vernal conjunctivitis and the following authors do not even mention it: Fuchs (Tratado de oftalmología Barcelona, Editorial

Labor S A, 1936, p 206), Berens (The Eye and Its Diseases, Philadelphia, W B Saunders Company, 1936, pp 404-407), May (Manuel des maladies de l'œil, Paris, Masson & Cie, 1936, p 162), and Romer (Tratado de oftalmología, Barcelona, Manuel Marín, Editor, 1932, p 162). Other authors have stated the belief that allergy does not explain all cases of the disease. Gifford (A Hand-Book of Ocular Therapeutics, ed 3, Philadelphia, Lea & Febiger, 1942, pp 238-240), citing Lemoine, stated this opinion. Ridley and Sorsby (Modern Trends in Ophthalmology, London, Butterworth & Co, Inc, 1940, p 9) asserted "Nevertheless, in the present state of our knowledge, the allergic basis of vernal conjunctivitis cannot be fully conceded." In light of these assertions, it is difficult to understand Dr Lehrfeld's lament that the ARCHIVES have given "conspicuous space to an article purporting to refute a recognized fact." As the chief editor accepted my manuscript, he apparently considered it worthy of publication, and it is precisely to the selection of its articles that the ARCHIVES owes its unquestioned prestige.

Dr Lehrfeld is right in saying that there are certain differences in vernal conjunctivitis in different regions. In the part of northern Mexico from which I wrote, the disease is seldom encountered in its most severe form, and in general it is characterized by the subjective symptoms of itching, sensation of heat or of a foreign body (such as dust) in the eyes and mild photophobia. The objective changes are presented in the tarsal conjunctiva and in the sclerocorneal limbus and its vicinity, while the rest of the bulbar conjunctiva and the fornix are normal. On the other hand, in Hawaii, where the thermometer never goes lower than about 60 F in the wintertime, the problem of treating vernal catarrh is an annoying and difficult one. There the disease occurs in its severest and most exaggerated form, and often the under surface of the upper lid is filled with hard, "cobble-stone" masses, which continually keep the eye irritated (Dr G M Van Poole, in a personal communication).

Unfortunately, in Mexico, there are lacking the support and organization necessary to maintain hospitals and research institutions with facilities which permit the carrying out of a well documented scientific investigation, for this reason, I have been unable to obtain any data on the amount of riboflavin in the urine of my patients. As I said before, my theory is based only on the results obtained by treatment with



riboflavin of patients with vernal conjunctivitis, and I leave to others its scientific confirmation.

Finally, quoting from the bulletin of the National Research Council, Dr Lehrfeld states that recession of the lesions of chronic ariboflavinosis is very slow, and he concludes by pointing out to the readers of the ARCHIVES that relief of ariboflavinosis is not as prompt as I have reported in patients with vernal conjunctivitis. For my part, I wish to note that the bulletin does not mention the severity of the chronic ariboflavinosis to which it refers, and that there is a great deal of difference between a slight and a severe lack of riboflavin, relief of the second deficiency being slower than that of the first. Connors, Eckardt and Johnson (Riboflavin for Rosacea Keratitis, Marginal Corneal Ulcers

and Corneal Infiltrates, ARCH OPHTH 29 956 [June] 1943) stated

After three or four daily intravenous injections of riboflavin, these infiltrates and the capillaries disappear, with relief of symptoms, even though a coexisting blepharoconjunctivitis remains unchanged clinically.

In the latter two conditions [rosacea keratitis and catarrhal ulcers], riboflavin simply reduces the duration of symptoms from one or two weeks to one or two days.

I wish to thank Dr Louis Lehrfeld for the interest he has taken in opposing my theory, it proves to me that in the scientific world there are men who defend not a theory but their own infallibility.

LUIS CASTELLANOS A, M D

Aldama 112, Chihuahua, Mexico

## News and Notes

### GENERAL NEWS

**Research Study Club of Los Angeles**—The Research Study Club of Los Angeles announces its fourteenth annual midwinter postgraduate clinical convention in ophthalmology and otolaryngology, to be held from Jan 22 to Feb 2, 1945. A special course in "Applied Anatomy and Cadaver Surgery of the Head and Neck" will be given February 2, 3, 4, 5 and 6 inclusive. Instructors and lecturers include C S O'Brien, M D, Iowa City, Kenneth Swan, M D, Portland, Ore, William Crisp, M D, Denver, John Shea, M D, Memphis, Tenn, Hans Brunner, M D, Chicago, Guy Lee Boyden, M D, Portland, Ore, Chauncey D Leake, M D, Galveston, Texas, Verne O Knudsen, Ph D, Los Angeles, and Scott Reger, Ph D, Iowa City. Applicants for the course should write to Pierre Viole, M D, 1930 Wilshire Boulevard, Los Angeles 5, Calif.

**Collection of Historic Tonometers**—The tonometer checking station at the Illinois Eye and Ear Infirmary is making a collection of historic tonometers. Will any reader who has a tonometer of interest for this collection donate

it for display? Credit will be shown. Any descriptive letters of such tonometers will be appreciated. Address Dr Harry S Gradle, 58 East Washington Street, Chicago appreciated.

**Course on Extraocular Muscles**—Dr James W White, of New York, will give a course on the extraocular muscles, with demonstrations, Dec 9 to 16, 1944, inclusive, at Northwestern University Medical School, 303 East Chicago Avenue, Chicago.

For further information, address Dr B Cushman, 25 East Washington Street, Chicago.

### SOCIETY NEWS

**Ophthalmological Society of Egypt**—To encourage scientific ophthalmic work the Ophthalmological Society of Egypt will award a gold medal with a value of 20 Egyptian pounds for the most valuable contribution of the year. The competition is open to all members of the society who have practiced less than twenty years, whether staying in or outside Egypt. In the event that no work is found of sufficient merit, an award shall not be made.

## Obituaries

### WILLIAM THORNWALL DAVIS, M D 1877-1944

William Thornwall Davis died at his home in Washington Friday, Feb 16, 1944, at the age of 67. He went as he would probably have wished, suddenly in the midst and at the peak of his brilliant, varied and fruitful career.

General Leonard Wood Dr Edmund Spaeth emphasizes the close contact that he maintained with the officers and with many enlisted men, especially those connected with the capture of Aguinaldo. In 1943 he was appointed consultant



WILLIAM THORNWALL DAVIS, M D  
1877-1944

Thornwall Davis (Bill to his intimates), of distinguished southern lineage, was born at Little Rock, Ark. By descent from an associate of George Rogers Clark, he held membership in the Society of the Cincinnati of Virginia. He was a nephew of Senator Blackburn of Kentucky and felt strong ties with that state, where he attended the Kentucky Military Institute. After receiving the degree of Doctor of Medicine from George Washington University and attending the United States Army Medical School, he began a notable career in the Army Medical Corps. This carried him through the Philippine campaign, where he served at one time under

to the Surgeon General of the United States Army.

In 1906 and 1912 postgraduate work at the University of Vienna and at the Royal Ophthalmic Hospital in London led to his receiving a professorship of ophthalmology during World War I in the Army Medical School, with the rank of major, and later, in 1920, at George Washington University. Here he gained immediate eminence. Not only was he a competent clinician, much sought in a rapidly expanding community, but he was also a gifted teacher. Mrs Davis writes "In the teaching of his students he gave them more than knowledge



He taught them love of service and integrity." His desire to reach a larger field in education brought about the inception of the famed George Washington University postgraduate course in ophthalmology. This was one of the earliest and most influential of the so-called refresher courses. Organized with the military precision characterizing Dr. Davis' enterprises, it operated with amazing smoothness. The quality of the curriculum and his ability to select and attract lecturers brought to the course as students leaders in the specialty from long distances and many states. A large proportion took the course year after year. Dr. Davis devised the unique plan of transcribing the lectures in the course to make them available for the students. This furnished a permanent record of original and valuable material and provided a useful and prized textbook.

One of the earlier oculists to appreciate the significance of orthoptic methods, he equipped his office elaborately both in apparatus and in personnel. He also made this a distinctive feature of the graduate course, continued after other activities had been curtailed by the war.

Well groomed, able, shrewd, civic minded, he served in numerous local organizations. He was senior surgeon at the Episcopal Eye and Ear Hospital, chief of service in ophthalmology at the George Washington University Hospital and consultant to other hospitals. He was a member of the Rotary Club, which granted him funds to establish an orthoptic clinic at the Episcopal Eye and Ear Hospital, and a director of the Washington Loan and Trust Company and of the Washington Society for the Prevention of Blindness.

He was convinced of the importance of medical meetings as an essential factor in professional training and was a regular attendant at such gatherings in all parts of the country. He contributed important papers, especially in the field of ocular motility, reporting investigations of the oblique muscles and orthoptics, and served in positions of influence. He was president of the Washington Ophthalmological Society, first vice president of the American Academy of Ophthalmology and Oto-Laryngology and chairman of the executive committee of the council of the Southern Medical Association. He frequently took part in the examination of candidates for the certificate of the American Board of Ophthalmology, and from his position in Washington he was a valued counsellor and supporter of the Board. He was honored by membership in a host of national and foreign military and professional organizations and in 1940 was decorated with the Order of Carlos J. Finlay. Ingenious and constructive in meeting the problems presented by the various enterprises with which he was connected, his advice and assistance will be missed by many students and colleagues.

In 1912 he married Renee Tolson, who shared with him in the gracious hospitality of their delightful home. She survives him, with four sons: Dr. William J. G. Davis, Cleveland, Major Roger Hasbrouck Davis, Army Air Forces, First Lieutenant Rene S. Davis, United States Army, and Akin Thornwall Davis, a premedical student at George Washington University.

S. JUDD BEACH, M.D.

## Book Reviews

**The Principles and Practice of Ophthalmic Surgery.** Third Edition. By Edmund B. Spaeth, M.D. Price, \$11. Pp. 934, illustrated with 556 engravings, containing 798 figures and 6 colored plates. Philadelphia: Lea & Febiger, 1944.

In the third edition of this popular textbook on ophthalmic surgery one finds comparatively few changes. Most of the chapters have been altered little, if any. The section on muscles properly includes a discussion on the development of squint and its nonsurgical treatment. This chapter has largely been drawn from the writings of Travers and others who have made a special study of this subject. The author's great interest in ptosis is evidenced by the completeness with which this difficult problem has been covered. The section on intraocular foreign bodies has been largely rewritten, but it still leaves much to be desired. No mention

is made of the bone-free method of localizing foreign bodies. There is a good discussion on the present day method of dealing with malignant growths in and about the eye, and although the reviewer is not ready as yet to accept the author's assertion that "under ordinary circumstances, malignancy about the eye should be treated by radium therapy," the statement does portray the trend of the times. This well printed volume is replete with illustrations, most of which are excellently reproduced, but some are poor and meaningless. In spite of these minor criticisms, this textbook continues to fill an important place in ophthalmic literature. This edition has been reedited and revised, so its popularity is assured. It can be recommended to every ophthalmologist as a book of reference in which can be found definite advice on various surgical procedures.

JOHN H. DUNNINGTON

# Directory of Ophthalmologic Societies \*

## INTERNATIONAL

### INTERNATIONAL ASSOCIATION FOR PREVENTION OF BLINDNESS

President Dr P Baillart, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France

Secretary-General Prof M Van Duyse, Université de Gand, Gand, Prov Ostflandern, Belgium

All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France

### INTERNATIONAL OPHTHALMOLOGIC CONGRESS

President Prof Nordenson, Serafimerlasarettet, Stockholm, Sweden

Secretary Dr Ehlers, Jerbanenegade 41, Copenhagen, Denmark

### INTERNATIONAL ORGANIZATION AGAINST TRACHOMA

President Dr A F MacCallan, 17 Horseferry Rd, London, England

### PAN-AMERICAN CONGRESS OF OPHTHALMOLOGY

President Dr Harry S Gradle, 58 E Washington St, Chicago

Executive Secretaries Dr Conrad Berens, 35 E 70th St, New York Dr M E Alvaro, 1511 Rua Consolacão, São Paulo, Brazil

## FOREIGN

### ALL-INDIA OPHTHALMOLOGICAL SOCIETY

President Dr B K Narayan Rao, Minto Ophthalmic Hospital, Bangalore

Secretary Dr G Zachariah, Flitcham, Marshall's Rd, Madras

### BRITISH MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President Dr W Clark Souter, 9 Albyn Pl, Aberdeen, Scotland

Secretary Dr Frederick Ridley, 12 Wimpole St, London, W 1

### CHENG TU OPHTHALMOLOGICAL SOCIETY

President Dr Eugene Chan

Secretary Dr K S Sun

Place Eye, Ear, Nose and Throat Hospital, Chengtu, China

### CHINESE OPHTHALMOLOGY SOCIETY

President Dr C H Chou, 363 Avenue Haig, Shanghai

Secretary Dr F S Tsang, 221 Foochow Rd, Shanghai

### CHINESE OPHTHALMOLOGICAL SOCIETY OF PEIPING

President Dr H T Pi, Peiping Union Medical College, Peiping

Secretary Dr C K Lin, 180 Hsi-Lo-yen Chienmeng, Peiping

Place Peiping Union Medical College, Peiping Time Last Friday of each month

### GERMAN OPHTHALMOLOGICAL SOCIETY

President Prof W Lohlein, Berlin

Secretary Prof E Engelking, Heidelberg

### HUNGARIAN OPHTHALMOLOGICAL SOCIETY

President Prof I Imre, Budapest

Assistant Secretary Dr Stephen de Grosz, University Eye Hospital, Mariautca 39, Budapest

All correspondence should be addressed to the Assistant Secretary

## MIDLAND OPHTHALMOLOGICAL SOCIETY

President Dr W Niccol, 4 College Green, Gloucester, England

Secretary Mr T Harrison Butler, 61 Newhall St, Birmingham 3, England

Place Birmingham and Midland Eye Hospital

## NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President Mr John Foster, 45 Park Sq, Leeds, England

Secretary Mr William M Muirhead, 70 Upper Hanover St, Sheffield, England

Place Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation Time October to April

## OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President Dr A James Flynn, 135 Macquarie St, Sydney

Secretary Dr D Williams, 193 Macquarie St, Sydney

## OPHTHALMOLOGICAL SOCIETY OF EGYPT

President Prof Dr Mohammed Mahfouz Bey, Government Hospital, Alexandria

Secretary Dr Mohammed Khalil, 4 Baehler St, Cairo

All correspondence should be addressed to the secretary, Dr Mohammed Khalil

## OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President Mr Charles B Goulden, OBE, MD, MCh, 89 Harley St, London, England

Secretary Mr Frank W Law, MA, MD, FRCS, 30 Devonshire Pl, London W 1, England

## OPHTHALMOLOGY SOCIETY OF BOMBAY

President Dr D D Sathaye, 127 Girgaum Rd, Bombay 4, India

Secretary Dr H D Dastur, Dadar, Bombay 14, India

Place H B A Free Ophthalmic Hospital, Parel, Bombay 12 Time First Friday of every month

## OXFORD OPHTHALMOLOGICAL CONGRESS

Master Mr P G Doyne, 60 Queen Anne St, London, W 1, England

Secretary-Treasurer Dr F A Anderson, 12 St John's Hill, Shrewsbury, England

Place Oxford, England Time July 8-9, 1943

## PALESTINE OPHTHALMOLOGICAL SOCIETY

President Dr Arich Feigenbaum, Abyssinian St 15, Jerusalem

Secretary Dr E Sinai, Tel Aviv

## POLISH OPHTHALMOLOGICAL SOCIETY

President Dr W Kapuściński, 2 Waly Batorego, Poznan

Secretary Dr J Sobański, Lindley'a 4, Warsaw

Place Lindley'a 4 Warsaw

## ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President Col F A Juler, 96 Harley St, London, W 1, England

Secretary Dr Harold Ridley, 60 Queen Anne St, London, W 1, England

\* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date

## SÃO PAULO SOCIETY OF OPHTHALMOLOGY

President Prof Moacyr E Alvaro, Consolação 1151, São Paulo, Brazil  
 Secretary Dr Silvio de Almeida Toledo, Enfermaria Santa Luzia, Santa Casa de Misericórdia, Cesario Motta, St 112, São Paulo, Brazil

## SCOTTISH OPHTHALMOLOGICAL CLUB

President Dr S Spence Meighan, 13 Woodside Pl, Glasgow, C 3  
 Secretary Dr Alexander Garrow, 15 Woodside Pl, Glasgow, C 3  
 Place Edinburgh and Glasgow, in rotation

## SOCIEDAD ARGENTINA DE OFTALMOLOGIA

Chairman Dr Jorge Malbran, Buenos Aires  
 Secretary Dr Benito Just Tiscornia, Santa Fe 1171, Buenos Aires

## SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President Prof Dr Carlos Weskamp, Laprida 1159, Rosario  
 Secretary Dr Juan M Vila Ortiz, Cordoba 1433, Rosario  
 Place Rosario Time Last Saturday of every month, April to November, inclusive All correspondence should be addressed to the President

## SOCIEDADE DE OFTALMOLOGIA DE MINAS GERAIS

President Prof Hilton Rocha, Rua Rio de Janeiro 2251, Belo Horizonte, Minas Gerais  
 Secretary Dr Ennio Coscarelli, Rua Aimores 1697, Belo Horizonte, Minas Gerais

## SOCIEDADE DE OFTALMOLOGIA E OTORRINOLARINGOLOGIA DE RIO GRANDE DO SUL

President Dr Luiz Assumpção Osorio, Edifício Vera Cruz, Apartamento 134, Porto Alegre, Rio Grande do Sul  
 Secretary Dr Fernando Voges Alves, Caixa Postal 928, Porto Alegre, Rio Grande do Sul

## SOCIEDADE DE OPHTHALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President Dr Theonilo Amorim, Barra Avenida, Bahia, Brazil  
 Secretary Dr Adroaldo de Alencar, Brazil  
 All correspondence should be addressed to the President

## SOCIETA OFTALMOLOGICA ITALIANA

President Prof Dott Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome  
 Secretary Prof Dott Epimaco Leonardi, Via del Gianicolo, 1, Rome

## SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary Dr Rene Onfray, 6 Avenue de la Motte Picquet, Paris, 7<sup>e</sup>

## SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President Prof K G Ploman, Stockholm  
 Secretary Dr K O Granstrom, Södermalmstorg 4 Ill tr, Stockholm, So

## TEL AVIV OPHTHALMOLOGICAL SOCIETY

President Dr D Arieh-Friedman, 96 Allenby St, Tel Aviv, Palestine.  
 Secretary Dr Sadger Max, 9 Bialik St, Tel Aviv, Palestine

## NATIONAL

## AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman Dr Frederick C Cordes, 384 Post St, San Francisco  
 Secretary Dr R J Masters, 23 E Ohio St, Indianapolis

## AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President Dr Lawrence T Post, Metropolitan Bldg, St Louis  
 President-Elect Dr Gordon B New, Mayo Clinic, Rochester, Minn  
 Executive Secretary-Treasurer Dr William L Benedict, 101-1st Ave Bldg, Rochester, Minn

## AMERICAN OPHTHALMOLOGICAL SOCIETY

President Dr S Judd Beach, 704 Congress St, Portland, Maine  
 Secretary-Treasurer Dr Walter S Atkinson, 129 Clinton St, Watertown, N Y

## ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC

Chairman Dr Conrad Berens, 35 E 70th St, New York  
 Secretary-Treasurer Major Brittain F Payne, School of Aviation Medicine, Randolph Field, Texas  
 Assistant Secretary-Treasurer Dr Hunter Romaine, 35 E 70th St, New York

## CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President Dr Alexander E MacDonald, 170 St George St, Toronto  
 Secretary-Treasurer Dr L J Sebert, 170 St George St, Toronto

## CANADIAN OPHTHALMOLOGICAL SOCIETY

President Dr R Evatt Mathers, 34½ Morris St, Halifax, N S  
 Secretary-Treasurer Dr Kenneth B Johnston, Suite 1, 1509 Sherbrooke St W, Montreal

## NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President Mr Mason H Bigelow, 1790 Broadway, New York  
 Secretary Miss Regina E Schneider, 1790 Broadway, New York  
 Executive Director Mrs Eleanor Brown Merrill, 1790 Broadway, New York

## SECTIONAL

## ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President Dr N Zwaifler, 46 Wilbur Ave, Newark  
 Secretary Dr William F Keim Jr, 25 Roseville Ave, Newark  
 Place 91 Lincoln Park South, Newark. Time 8 45 p m, second Monday of each month, October to May

## CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr L J Friend, 425 E Grand Ave, Beloit, Wis  
 Secretary Dr G L McCormick, 626 S Central Ave, Marshfield

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President Dr Paul A Chandler, 5 Bay State Rd, Boston  
 Secretary-Treasurer Dr Merrill J King, 264 Beacon St, Boston  
 Place Massachusetts Eye and Ear Infirmary, 243 Charles St, Boston Time 8 p m, third Tuesday of each month from November to April, inclusive

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President Dr D H O'Rourke, 1612 Tremont Pl, Denver  
 Secretary-Treasurer Dr C Allen Dickey, 450 Sutter St, San Francisco

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr L L Bull, 1215-14th Ave, Seattle, Wash  
 Secretary-Treasurer Dr Barton E Peden, 301 Stimson Bldg, Seattle 1  
 Place Seattle or Tacoma, Wash Time Third Tuesday of each month except June, July and August

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President Dr J Sheldon Clark, 27 E Stephenson St, Freeport, Ill  
 Secretary-Treasurer Dr Harry R Warner, 321 W State St, Rockford, Ill  
 Place Rockford, Ill, or Janesville or Beloit, Wis Time Third Tuesday of each month from October to April, inclusive

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr M H Pike, Midland, Mich  
 Secretary-Treasurer Dr H H Heuser, 207 Davidson Bldg, Bay City, Mich  
 Place Saginaw or Bay City, Mich Time Second Tuesday of each month, except July, August and September

SIoux VALLEY EYE AND EAR ACADEMY

President Dr J C Decker, 515 Francis Bldg, Sioux City, Iowa  
 Secretary-Treasurer Dr J E Dvorak, 408 Davidson Bldg, Sioux City, Iowa

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman Dr John H Burleson, 414 Navarro St, San Antonio, Texas  
 Secretary Dr J W Jervey Jr, 101 Church St, Greenville, S C

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President Dr H L Brehmer, 221 W Central Ave, Albuquerque, N Mex  
 Secretary Dr A E Cruthirds, 1011 Professional Bldg, Phoenix, Ariz

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President Dr W M Dodge, 716 First National Bank Bldg, Battle Creek  
 Secretary-Treasurer Dr Kenneth Lowe, 25 W Michigan Ave, Battle Creek  
 Time Last Thursday of September, October, November, March, April and May

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Ray Parker, 218 Franklin St, Johnston, Pa  
 Secretary-Treasurer Dr J McClure Tyson, Deposit Nat'l Bank Bldg, DuBois

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President Dr Raymond C Cook, 701 Main St, Little Rock  
 Secretary Dr K W Cosgrove, Urquhart Bldg, Little Rock

COLORADO OPHTHALMOLOGICAL SOCIETY

President Dr C A Ringle, 912-9th Ave, Greeley  
 Secretary Dr W A Ohmart, 1102 Republic Bldg, Denver  
 Place University Club, Denver Time 7 30 p m, third Saturday of each month, October to May, inclusive

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President Dr F L Phillips, 405 Temple St, New Haven  
 Secretary-Treasurer Dr W H Turnley, 1 Atlantic St, Stamford, Conn

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President William O Martin Jr, Doctors Bldg, Atlanta  
 Secretary-Treasurer Dr C K McLaughlin, 526 Walton St, Macon

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr F McK Ruby, Union City  
 Secretary Dr Edwin W Dyar Jr, 23 E Ohio St, Indianapolis  
 Place French Lick Time First Wednesday in April

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr J K Von Lackum, 117-3d St S E, Cedar Rapids  
 Secretary-Treasurer Dr B M Merkel, 604 Locust St, Des Moines

KANSAS STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr W D Pittman, Pratt  
 Secretary Dr Louis R Haas, 902 N Broadway, Pittsburg

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr Val H Fuchs, 200 Carondelet St, New Orleans  
 Secretary-Treasurer Dr Edley H Jones, 1301 Washington St, Vicksburg, Miss

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr Robert H Fraser, 25 W Michigan Ave, Battle Creek  
 Secretary Dr R G Laird, 114 Fulton St, Grand Rapids

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr George E McGeary, 920 Medical Arts  
Bldg, Minneapolis  
Secretary Dr William A Kennedy, 372 St. Peter St,  
St Paul  
Time Second Friday of each month from October to  
May

## MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President Dr William Morrison, 208 N Broadway,  
Billings, Mont  
Secretary Dr Fritz D Hurd, 309 Medical Arts Bldg,  
Great Falls

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr W Howard Morrison, 1500 Medical  
Arts Bldg, Omaha  
Secretary-Treasurer Dr John Peterson, 1307 N St  
Lincoln

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON  
OPHTHALMOLOGY, OTOTOLOGY AND  
RHINOLARYNGOLOGY

Chairman Dr B E Failing, 31 Lincoln Park, Newark  
Secretary Dr George Meyer, 410 Haddon Ave,  
Camden

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR,  
NOSE AND THROAT SECTION

Chairman Dr Harold J Joy, 504 State Tower Bldg,  
Syracuse 2  
Secretary Dr Maxwell D Ryan, 660 Madison Ave,  
New York 21

NORTH CAROLINA EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr Hugh C Wolfe, 102 N Elm St,  
Greensboro  
Secretary Dr Vanderbilt F Couch, 104 W 4th St,  
Winston-Salem

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY  
AND OTO-LARYNGOLOGY

President Dr W L Diven, City National Bank Bldg,  
Bismarck  
Secretary-Treasurer Dr A E Spear, 20 W Villard,  
Dickenson

OREGON ACADEMY OF OPHTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr Paul Neely, 1020 S W Taylor St,  
Portland  
Secretary-Treasurer Dr Lewis Jordon, 1020 S W  
Taylor St, Portland  
Place Good Samaritan Hospital, Portland Time  
Third Tuesday of each month

PENNSYLVANIA ACADEMY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr Lewis T Buckman, 83 S Franklin St,  
Wilkes-Barre  
Secretary Pro Tem Dr Paul C Craig, 232 N 5th  
St, Reading  
Time Last week in April

RHODE ISLAND OPHTHALMOLOGICAL AND  
OTOLOGICAL SOCIETY

Acting President Dr N Darrell Harvey, 112 Water-  
man St, Providence  
Secretary-Treasurer Dr Linley C Happ, 124 Water-  
man St, Providence  
Place Rhode Island Medical Society Library, Provi-  
dence Time 8 30 p m, second Thursday in  
October, December, February and April

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY  
AND OTOLARYNGOLOGY

President Dr J L Sanders, 222 N Main St, Green-  
ville  
Secretary Dr J H Stokes, 125 W Cheves St,  
Florence

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr Wesley Wilkerson, 700 Church St,  
Nashville  
Secretary-Treasurer Dr W D Stinson, 124 Physicians  
and Surgeons Bldg, Memphis

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL  
SOCIETY

President Dr F H Rosebrough, 603 Navarro St,  
San Antonio  
Secretary Dr M K McCullough, 1717 Pacific Ave,  
Dallas

## UTAH OPHTHALMOLOGICAL SOCIETY

President Dr R B Maw, 699 E South Temple, Salt  
Lake City  
Secretary-Treasurer Dr Charles Ruggeri Jr, 1120  
Boston Bldg, Salt Lake City  
Place University Club, Salt Lake City Time 7 00  
p m, third Monday of each month

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND  
OPHTHALMOLOGY

President Dr Mortimer H Williams, 30½ Franklin  
Rd S W, Roanoke  
Secretary-Treasurer Dr Meade Edmunds, 34 Franklin  
St, Petersburg

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE,  
EAR, NOSE AND THROAT SECTION

President Dr George Traugh, 309 Cleveland Ave,  
Fairmont  
Secretary Dr Welch England, 621½ Market St,  
Parkersburg

## LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr E L Mather, 39 S Main St, Akron,  
Ohio  
Secretary-Treasurer Dr V C Malloy, 2d National  
Bank Bldg, Akron, Ohio  
Time First Monday in January, March, May and  
November

## ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr B M Cline, 153 Peachtree St N E,  
Atlanta, Ga  
Acting Secretary Dr A V Hallum, 478 Peachtree  
St N E, Atlanta, Ga  
Place Grady Hospital Time 6 00 p m, fourth Mon-  
day of each month, from October to May

BALTIMORE MEDICAL SOCIETY, SECTION ON  
OPHTHALMOLOGY

Chairman Dr Ernst Bodenheimer, 1212 Eutaw Pl,  
Baltimore  
Secretary Dr Thomas R O'Rourke, 104 W Madison  
St, Baltimore  
Place Medical and Chirurgical Faculty, 1211 Cathedral  
St Time 8 30 p m, fourth Thursday of each  
month from October to March

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President Each member, in alphabetical order  
Secretary Dr Luther E Wilson, 919 Woodward Bldg,  
Birmingham, Ala  
Place Tutwiler Hotel Time 6 30 p m, second  
Tuesday of each month, September to May, inclusive

BROOKLYN OPTHALMOLOGICAL SOCIETY

President Dr Michael J Buonaguro, 589 Lorimer St,  
Brooklyn  
Secretary-Treasurer Dr Benjamin C Rosenthal, 140  
New York Ave, Brooklyn 16  
Place Kings County Medical Society Bldg, 1313 Bed-  
ford Ave Time Third Thursday in February, April,  
May, October and December

BUFFALO OPTHALMOLOGIC CLUB

President Dr Walter F King, 519 Delaware Ave,  
Buffalo  
Secretary-Treasurer Dr Sheldon B Freeman, 196  
Linwood Ave, Buffalo  
Time Second Thursday of each month

CHATTANOOGA SOCIETY OF OPTHALMOLOGY AND  
OTOLARYNGOLOGY

President Each member, in alphabetical order  
Secretary Dr Douglas Chamberlain, Chattanooga  
Bank Bldg, Chattanooga, Tenn  
Place Mountain City Club Time Second Thursday  
of each month from September to May

CHICAGO OPTHALMOLOGICAL SOCIETY

President Dr Vernon M Leech, 55 E Washington  
St, Chicago  
Secretary Dr W A Mann, 30 N Michigan Ave,  
Chicago  
Place Chicago Towers Club, 505 N Michigan Ave  
Time Third Monday of each month from October  
to May

CINCINNATI GENERAL HOSPITAL OPTHALMOLOGY  
STAFF

Chairman Dr D T Vail, 441 Vine St, Cincinnati  
Secretary Dr A A Levin, 441 Vine St, Cincinnati  
Place Cincinnati General Hospital Time 7 45 p m,  
third Friday of each month except June, July and  
August

CLEVELAND OPTHALMOLOGICAL CLUB

Chairman Dr Shandor Monson, 1621 Euclid Ave,  
Cleveland  
Secretary Dr Carl Ellenberger, 14805 Detroit Ave,  
Cleveland  
Time Second Tuesday in October, December, February  
and April

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION  
ON OPTHALMOLOGY

Chairman Dr W S Reese, 1901 Walnut St,  
Philadelphia  
Clerk Dr George F J Kelly, 37 S 20th St,  
Philadelphia  
Time Third Thursday of every month from October  
to April, inclusive

COLUMBUS OPTHALMOLOGICAL AND OTO-  
LARYNGOLOGICAL SOCIETY

Chairman Dr H D Emswiler, 370 E Town St,  
Columbus, Ohio  
Secretary-Treasurer Dr D G Sanor, 206 E State  
St, Columbus, Ohio  
Place The Neil House Time 6 p m, first Monday  
of each month

CORPUS CHRISTI EYE, EAR, NOSE AND  
THROAT SOCIETY

Chairman Dr Arthur Padillo, 414 Medical Profes-  
sional Bldg, Corpus Christi, Texas  
Secretary Dr Edgar G Mathis, 815 Medical Arts  
Bldg, Corpus Christi, Texas  
Time Second Friday of each month from October to  
May

DALLAS ACADEMY OF OPTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr Ruby K Daniel, Medical Arts Bldg,  
Dallas 1, Texas  
Secretary Dr Tom Barr, Medical Arts Bldg, Dallas 1,  
Texas  
Place Dallas Athletic Club Time 6 30 p m, first  
Tuesday of each month from October to June The  
November, January and March meetings are devoted  
to clinical work

DES MOINES ACADEMY OF OPTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr H C Schmitz, 604 Locust St, Des  
Moines, Iowa  
Secretary-Treasurer Dr Byron M Merkel, 604 Locust  
St, Des Moines, Iowa  
Time 7 45 p m, third Monday of every month from  
September to May

DETROIT OPTHALMOLOGICAL CLUB

Chairman Members rotate alphabetically  
Secretary Dr Cecil W Lepard, 1025 David Whitney  
Bldg, Detroit  
Place Club rooms of Wayne County Medical Society  
Time First Wednesday of each month, November  
through April

DETROIT OPTHALMOLOGICAL SOCIETY

President Dr Parker Heath, 1553 Woodward Ave,  
Detroit  
Secretary Dr Leland F Carter, 1553 Woodward Ave,  
Detroit  
Place Club rooms of Wayne County Medical Society  
Time Third Thursday of each month from Novem-  
ber to April, inclusive

EASTERN NEW YORK EYE, EAR, NOSE AND  
THROAT ASSOCIATION

President Appointed at each meeting  
Secretary-Treasurer Dr Joseph L Holohan, 330 State  
St, Albany  
Time Third Wednesday in October, November, March,  
April, May and June

## FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Rex Howard, 602 W 10th St, Fort Worth, Texas  
 Secretary-Treasurer Dr R H Gough, Medical Arts Bldg, Fort Worth, Texas  
 Place Medical Hall, Medical Arts Bldg Time 7 30 p m, first Friday of each month except July and August

## HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SECTION

President Dr Lyle J Logue, 1304 Walker Ave, Houston, Texas  
 Secretary Dr John T Stough, 803 Medical Arts Bldg, Houston, Texas  
 Place Medical Arts Bldg, Harris County Medical Society Rooms Time 8 p m, second Thursday of each month from September to June

## INDIANAPOLIS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President Dr Myron Harding, 23 E Ohio St, Indianapolis  
 Secretary Dr Kenneth L Craft, 23 E Ohio St, Indianapolis  
 Place Indianapolis Athletic Club Time 6 30 p m, second Thursday of each month from November to May

## KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Edgar Johnson, 906 Grand Ave, Kansas City, Mo  
 Secretary Dr W E Keith, 1103 Grand Ave, Kansas City, Mo  
 Time Third Thursday of each month from October to June The November, January and March meetings are devoted to clinical work

## LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr Harold Snow, 614 S Pacific Ave, San Pedro, Calif  
 Secretary-Treasurer Dr Oliver R Nees, 508 Times Bldg, Long Beach, Calif  
 Place Professional Bldg Time Last Wednesday of each month from October to May

## LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr M E Trainor, 523 W 6th St, Los Angeles  
 Secretary-Treasurer Dr Orrie E Ghrist, 210 N Central Ave, Glendale, Calif  
 Place Los Angeles County Medical Association Bldg, 1925 Wilshire Blvd Time 6 00 p m, fourth Monday of each month from September to May, inclusive

## LOUISVILLE EYE AND EAR SOCIETY

President Dr Joseph S Heitger, Heyburn Bldg, Louisville, Ky  
 Secretary-Treasurer Dr J W Fish, 321 W Broadway, Louisville, Ky  
 Place Brown Hotel Time 6 30 p m, second Thursday of each month from September to May, inclusive

## LOWER ANTHRACITE EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Each member in alphabetical order  
 Secretary Dr James J Monohan, 31 S Jardin St, Shenandoah, Pa

## MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr P S Constantinople, 1835 I St N W, Washington  
 Secretary Dr Frazier Williams, 1801 I St N W, Washington  
 Place 1718 M St N W Time 8 p m, third Friday of each month from October to April, inclusive

## MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Each member in alphabetical order  
 Secretary Dr Sam H Sanders, 1089 Madison Ave, Memphis, Tenn  
 Place Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital Time 8 p m, second Tuesday of each month from September to May

## MILWAUKEE OTO-OPHTHALMIC SOCIETY

President Dr Edwin C Bach, 324 E Wisconsin Ave, Milwaukee  
 Secretary-Treasurer Dr Ralph T Rank, 238 W Wisconsin Ave, Milwaukee  
 Place University Club Time 6 30 p m, second Tuesday of each month

## MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman Dr H V Dutrow, 1040 Fidelity Medical Bldg, Dayton, Ohio  
 Secretary-Treasurer Dr Maitland D Place, 981 Reibold Bldg, Dayton, Ohio  
 Place Van Cleve Hotel Time 6 30 p m, first Tuesday of each month from October to June, inclusive.

## MONTREAL OPHTHALMOLOGICAL SOCIETY

President Dr J Rosenbaum, 1396 Ste Catherine St W, Montreal, Canada  
 Secretary Dr L Tessier, 1230 St Joseph Blvd E, Montreal, Canada  
 Time Second Thursday of October, December, February and April

## NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr M M Cullom, 700 Church St, Nashville, Tenn  
 Secretary Dr R E Sullivan, 432 Doctors Bldg, Nashville, Tenn  
 Place St Thomas Hospital Time 8 p m, third Monday of each month from October to May

## NEW HAVEN OPHTHALMOLOGICAL SOCIETY

President Dr William H Ryder, 185 Church St, New Haven, Conn  
 Secretary Dr Frederick A Wiess, 255 Bradley St, New Haven, Conn

NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr W B Clark, 1012 American Bank Bldg, New Orleans.  
Secretary Dr Mercer G Lynch, 1018 Maison Blanche Bldg, New Orleans  
Place Louisiana State University Medical Bldg  
Time 8 p m, second Tuesday of each month from October to May

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman Dr. Frank C Keil, 660 Madison Ave, New York  
Secretary Dr Willis S Knighton, 121 E 61st St, New York  
Time 8 30 p m, third Monday of every month from October to May, inclusive

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President Dr Milton Berliner, 57 W 57th St, New York  
Secretary Dr Benjamin Esterman, 983 Park Ave, New York  
Place Squibb Hall, 745-5th Ave Time 8 p m, first Monday of each month from October to May, inclusive

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr James P Luton, 117 N Broadway, Oklahoma City  
Secretary Dr Harvey O Randel, 117 N Broadway, Oklahoma City  
Place University Hospital Time Second Tuesday of each month from September to May

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr D D Stonecypher, Nebraska City, Neb  
Secretary-Treasurer Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha  
Place Omaha Club, 20th and Douglas Sts, Omaha  
Time 6 p m dinner, 7 p m program, third Wednesday of each month from October to May

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President Dr Thomas Sanfacon, 340 Park Ave, Paterson, N J  
Secretary-Treasurer Dr J Averbach, 435 Clinton Ave, Clinton, N J  
Place Paterson Eye and Ear Infirmary Time 9 p m, last Friday of every month, except June, July and August

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

President Dr Isaac Tassman, 136 S 16th St, Philadelphia  
Secretary Dr Glen Gregory Gibson, 255 S 17th St, Philadelphia  
Time First Thursday of each month from October to May

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President Dr George H Shuman, 351-5th Ave, Pittsburgh  
Secretary Dr Robert J Billings, 509 Liberty Ave, Pittsburgh  
Place Pittsburgh Academy of Medicine Bldg Time Fourth Monday of each month, except June, July, August and September

READING EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Michael J Penta, 312 N 5th St, Reading, Pa  
Secretary Dr Paul C Craig, 232 N 5th St, Reading, Pa  
Place Wyomissing Club Time 6 30 p m, third Wednesday of each month from September to July

RICHMOND OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr Peter N Pastore, Medical College of Virginia, Richmond, Va  
Secretary Dr Clifford A Folkes, Professional Bldg, Richmond, Va  
Place Westmoreland Club Time 6 p m, second Monday of each month from October to May

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Frank Barber, 75 S Fitzhugh St, Rochester, N Y  
Secretary-Treasurer Dr Charles T Sullivan, 277 Alexander St, Rochester, N Y

ST LOUIS OPHTHALMIC SOCIETY

President Dr C C Beisbarth, 3720 Washington Blvd, St Louis  
Secretary Dr H R Hildreth, 508 N Grand Blvd, St Louis  
Place Oscar Johnson Institute Time Clinical meeting, 5 30 p m, dinner and scientific meeting 6 30 p m, fourth Friday of each month from October to April, inclusive, except December

SAN ANTONIO OPHTHALMO-OTO-LARYNGOLOGICAL SOCIETY

President Dr Belvin Pritchett, 705 E Houston St, San Antonio 5, Texas  
Secretary-Treasurer Lt Col John L Matthews, AAF School of Aviation Medicine, Randolph Field, Texas  
Place San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center  
Time 7 p m, second Tuesday of each month from October to May

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman Dr Roy H Parkinson, 870 Market St, San Francisco  
Secretary Dr A G Rawlins, 384 Post St, San Francisco  
Place Society's Bldg, 2180 Washington St, San Francisco Time Fourth Tuesday of every month except June, July and December

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President Dr David C Swearingen, Slattery Bldg, Shreveport, La  
Secretary-Treasurer Dr Kenneth Jones, Medical Arts Bldg, Shreveport, La  
Place Shreveport Charity Hospital Time 7 30 p m, first Monday of every month except July, August and September



SPOKANE ACADEMY OF OPHTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr Clarence A Veasey Sr, 421 W River-  
side Ave, Spokane, Wash  
Secretary Dr Clarence A Veasey Jr, 421 W River-  
side Ave, Spokane, Wash  
Place Spokane Medical Library Time 8 p m, fourth  
Tuesday of each month except June, July and August

SYRACUSE EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr A H Rubenstein, 713 E Genesee St,  
Syracuse, N Y  
Secretary-Treasurer Dr I H Blaisdell, 713 E  
Genesee St, Syracuse, N Y  
Place University Club Time First Tuesday of each  
month except June, July and August

TOLEDO EYE, EAR, NOSE AND  
THROAT SOCIETY

Chairman Dr E W Campbell, 316 Michigan St,  
Toledo, Ohio  
Secretary Dr L C Ravin, 316 Michigan St, Toledo,  
Ohio  
Place Toledo Club Time Each month except June,  
July and August

TORONTO ACADEMY OF MEDICINE, SECTION OF  
OPHTHALMOLOGY

Chairman Dr W R F Luke, 316 Medical Arts Bldg,  
Toronto, Canada  
Secretary Dr W T Gratton, 216 Medical Arts Bldg,  
Toronto, Canada  
Place Academy of Medicine, 13 Queens Park Time  
First Monday of each month, November to April

WASHINGTON, D C, OPHTHALMOLOGICAL SOCIETY

President Dr S Bockoven, 1752 Massachusetts Ave,  
Washington, D C  
Secretary-Treasurer Dr John Lloyd, 1218-16th St  
N W, Washington, D C  
Place Medical Society of District of Columbia Bldg,  
1718 M St N W, Washington, D C Time 7 30  
p m, first Monday in November, January, March  
and May

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman Each member in turn  
Secretary Dr Samuel T Buckman, 70 S Franklin  
St, Wilkes-Barre, Pa  
Place Office of chairman Time Last Tuesday of  
each month from October to May

## LOCALIZATION OF INTRAOCULAR FOREIGN BODIES BY MEANS OF THE CONTACT LENS

RAYMOND L. PFEIFFER, M.D.

NEW YORK

The war and the war industries make the consideration of the treatment of intraocular foreign bodies opportune. Surgeons who heretofore have had little experience with intraocular foreign bodies are being called on to treat many injuries of this type. Roentgenologists likewise are feeling more poignantly their responsibility in this field. Naturally the question arises as to which methods of treatment are superior. After the use of various technics, I have found the procedures here described best adapted to the problem.

The choice of surgical procedure for the extraction of foreign bodies seems to be changing. Many surgeons with much experience in the handling of intraocular injuries are giving up the use of the giant magnet entirely, and others use it only in rare instances. The grosser technic of the giant magnet has not satisfied the surgeons' desire for refinement and has failed to produce results comparable to those achieved with the hand instrument. Success with the hand magnet, however, depends on accurate localization of the foreign body, so that it may be removed directly through the wall of the eye with a minimum of injury. Precise localization, therefore, is imperative.

Many methods for both localization and removal of intraocular fragments are available, and no unanimity of opinion on the superiority of this or that method exists, though it is probable that certain technics are definitely superior. There is no doubt, however, that ophthalmologists are dependent on roentgen examination for the diagnosis and localization of intraocular bodies. Although ophthalmoscopy is frequently of great value, it cannot be employed as a substitute for roentgen localization, even when the foreign fragment can be seen with an ophthalmoscope. It is not possible to locate a foreign body with the ophthalmoscope as accurately as by roentgen examination. Ophthalmoscopy is a valuable adjunct and should be used in every case

in addition to roentgen examination but not to replace it. With consummate care it is possible for a roentgenologist to localize a foreign fragment in the eye and to give the points of its position with greater accuracy than the surgeon can utilize at operation.

Unless the surgeon is careful the value of the good work of the roentgenologist may be lost. In applying the data on the position of the body in the eye the operator should mark the exact meridian in which the body lies with peripheral scratches on the cornea, stained with fluorescein, before making an incision. In locating the meridian, a Guss protractor is an important aid. If reliable localization is not available, the Berman locator may be used to determine the site for the incision if the particle is of iron or steel. If the fragment is far posterior and the meridian in which the fragment lies is difficult to trace posteriorly from the cornea, this remarkable instrument should be most helpful.

Ophthalmologists have generally assumed that the localization of intraocular particles is a task for the roentgenologist. In some communities the roentgenologists are so engrossed in general work that they have little interest in what may appear to be an annoying and trifling problem. With the methods to be presently described, an ophthalmic surgeon does not need to be altogether dependent on a roentgenologist. He should be equipped to take patients to an x-ray laboratory and prepared to direct the procedure. Certainly every recent graduate in ophthalmology should be able to locate intraocular fragments with complete assurance.

In every case of possible intraocular foreign body, bone-free roentgenograms should be made by Vogt's method (fig. 1).<sup>1</sup> Roentgenograms made by this method show far more than those made with rays which penetrate the bones of the skull, and they reveal bodies of almost any density greater than that of the soft tissues. Small

Read before the Academy of Medicine, New York, Dec. 20, 1943.

From the Institute of Ophthalmology, Presbyterian Hospital, and the Department of Ophthalmology, College of Physicians and Surgeons, Columbia University.

1 (a) Vogt, A. Skelettfreie Röntgenaufnahme des vorderen Bulbusabschnittes, Schweiz. med. Wchnschr. 51:145, 1921, (b) Weitere Beobachtungen über skelettfreie Röntgenaufnahme des vorderen Bulbusabschnittes, ibid. 4:982, 1923.

fragments of glass and minute metallic bodies whose shadows are lost in the grain of films exposed in the ordinary way can be shown. Bone-free roentgenograms are also valuable for determining the exact size and shape of bodies that have been localized on films exposed in the regular way. The more prominent the eye, the more useful is this method. An ordinary dental film is held over and perpendicular to the inner canthus of the eye, and the rays are directed from the side so that a shadow of the profile of the anterior segment of the eye, which includes the eyelids, the cornea and portions of the sclera, is recorded on the film. This method is useful

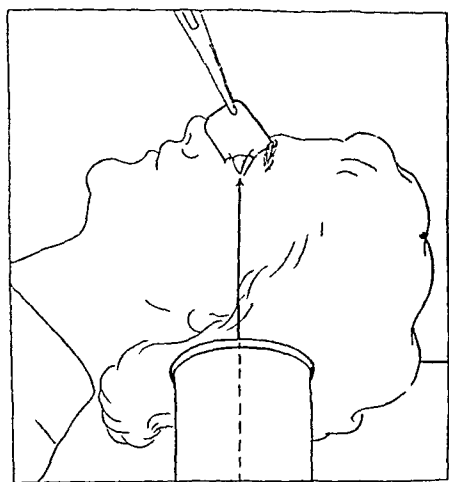


Fig 1—A drawing showing the position of the dental film held over the inner canthus for the production of a bone-free roentgenogram of the anterior segment of the eye

only for localizing fragments in the anterior 8 to 12 mm of the eye. Although the procedure is used primarily for diagnosis, it may be employed to localize foreign bodies by directing the rays from various angles onto dental films marked with pencil lines aligned with the limbus or the apex of the cornea. The position of the body is noted with reference to the lines on the roentgenograms, the shadow of the limbus or of the apex of the cornea and the angle at which the rays were directed toward the films.

All mechanical devices available for use in roentgen examination to determine the position of a foreign body in the eye use as a point of reference some definite part of the anterior segment, either the apex of the cornea or the plane of the limbus of the cornea. For this reason a fragment localized in or on the posterior sclera may be either in or out of the eyeball, depending on the size of the eyeball. A knowledge of the refraction of the eye is helpful. The position may be determined by injecting air into Tenon's capsule<sup>2</sup> and exposing films in such a manner that

the rays pass in a line tangential to the sclera adjacent to the point at which the foreign body is known to lie.

Eyes in which more than one fragment is found pose a particularly difficult problem. Several pellets of equal size and shape may be impossible to differentiate and localize.

The method of localization of foreign bodies which is probably superior to all others is that which employs the contact lens (fig 2). The technic of this method is simple. It provides two roentgenograms, a posteroanterior and a lateral which permit a meridional report, which is the easiest for the surgeon to use when operating. The method of localization is rapid, requires a minimum of apparatus and is applicable in all cases. Its outstanding advantage, however, is accuracy. It achieves a degree of accuracy which cannot be approached by five other methods with which I have had experience. It is not possible to make a gross error with this method, in all instances in which the contact lens fits the eye, the body is localized precisely, not just within a few millimeters, which is the margin of error claimed for most of the other methods. It seems safe to predict that in the course of time this method will replace all others.

Comberg<sup>3</sup> in 1927 adapted the Zeiss contact lens for the localization of foreign bodies. Prior to that date Wessely<sup>4</sup> used a glass prosthesis with tinfoil markers and later a crystal prosthesis that fitted on the eyeball. These prostheses, however, gave only a clue to the position of the globe, because they did not fit the eye well or

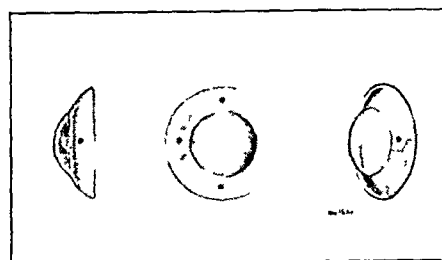


Fig 2—The contact lens especially adapted for roentgenographic localization of intraocular foreign bodies by the addition of four radiopaque markers (from Pfeiffer<sup>6</sup>)

3 (a) Comberg, W. Ein neues Verfahren zur Röntgenlokalisation am Augapfel, *Arch f Ophth* **118** 175, 1927, (b) Ein Hilfsgerät für mein Verfahren der Röntgenlokalisation und einige Bemerkungen über die Technik, *ibid* **124** 665, 1930.

4 (a) Wessely, K. Verfahren zur Lokalisation von metallischen intraocularen Fremdkörpern im Röntgenbilde, *Ztschr f Augenh*, 1910, vol 24, (b) Ein Verfahren zur Kenntlichmachung der Bulbusoberfläche und der Hornhaut im Röntgenbilde zwecks Lokalisierung von intraocularen Fremdkörpern, *Arch f Augenh* **69** 161, 1911.

2 Spackman E W. X-Ray Diagnosis of Double Perforation of Eyeball After Injection of Air into the Space of Tenon, *Am J Ophth* **15** 1007, 1932.

follow its movements. Later they were sewed to the conjunctiva, and other disadvantages were thus introduced. Then Engelbrecht<sup>5</sup> designated the cornea with balls of celluloid with wire crosses, which answered most requirements successfully. The contact glass of Comberg, in which the limbus of the cornea is designated by lead markers, fits tightly and moves with the eye. It is a lens of the type used for the correction of visual defects, and if the central visual acuity of the injured eye is not disturbed it is possible for the eye to fixate with the prosthesis in place. A lens of average size is used, that is, one with a

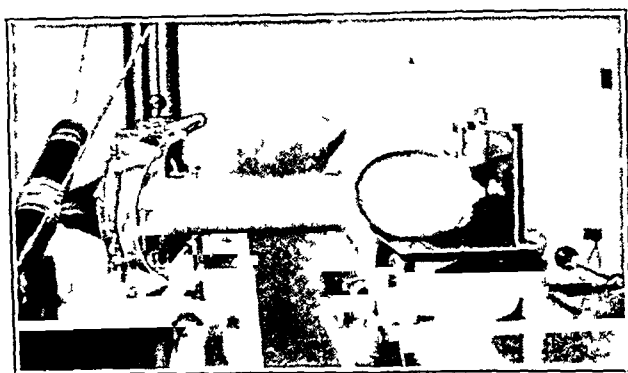


Fig 3—The arrangement of the apparatus for the posteroanterior exposure. The patient is in position, with the contact lens on the right eye. Note the perfect lateral position of the patient's head, with the chin and nose against the vertical tunnel. Immobilization is gained by biting a bar attached to the L-shaped device. (From Pfeiffer<sup>6</sup>)

radius of 12 mm for the scleral curve and of 8 mm for the corneal curve. The lens may be inserted and removed with ease. When it has been sterilized, it may be used on a lacerated globe with impunity. Lenses of this type are manufactured in the United States of plastic material.

Two roentgen exposures are made, a lateral and an anteroposterior. Lines are drawn on the films to show the relationship of the foreign particle to the contact lens. The location is then indicated on charts that represent an anteroposterior view of the eye and a cross section cut in the meridian in which the foreign body lies.

In order to shorten the time required for the projections and to remove one source of error, I have adapted a special device, which is not, however, indispensable to the method<sup>6</sup>. The device consists of an L-shaped arrangement of tunnels to hold the cassettes, with this device the patient's head may be maintained in one

position and the position of the tube changed between the two exposures.

#### PROCEDURE OF OBTAINING THE ROENTGENOGRAMS

The eye containing the intraocular foreign body is anesthetized with several drops of 0.5 per cent solution of tetracaine hydrochloride. The patient is directed to look down, and the contact lens is inserted by slipping the glass under the upper lid and lifting the lower lid. The lens finds its proper position over the cornea.

Two exposures are made, a posteroanterior and a lateral. The L-shaped device is placed on the roentgenographic table, and the positions of the tube for the two exposures are determined (fig 3). In both positions the primary rays are directed perpendicular to the surface of a tunnel so that they pass through the eye containing the foreign body. The target-film distance is the same for each exposure, a distance of 35 to 40 inches (90 to 100 cm) should be used.

The exposure for the posteroanterior view is made first. A patient with a foreign body in the right eye is instructed to lie on the table on his



Fig 4—The arrangement of the apparatus for the right lateral exposure, the film is placed in the horizontal tunnel. Note the alignment of the tube with the right orbit. The position of the contact lens can be checked through the apertures in the vertical tunnel. (From Pfeiffer<sup>6</sup>)

right side, with the right side of the head on the horizontal tunnel of the device. The tube is aligned in the horizontal position (fig 3). The head is placed so that the sagittal plane is horizontal and the injured eye is opposite the lower opening in the vertical tunnel. Through the opening in the vertical tunnel the position of the contact lens on the eye is checked, and the glass

<sup>5</sup> Engelbrecht, in Hoffmann, W. *Die Röntgendiagnostik und Therapie in der Augenheilkunde, Radiologische praktika*, Leipzig, Georg Thieme, 1932, vol 19.

<sup>6</sup> Pfeiffer, R. L. Localization of Intraocular Foreign Bodies with the Contact Lens, *Am J Roentgenol* 44: 558, 1940.

is rotated to place the markers in the vertical and horizontal planes. The patient is asked to gaze directly forward and to hold this position. To immobilize the head the patient may bite a bar attached to the L-shaped device. The position of the tube is checked, the cassette is placed in position in the vertical tunnel, and the posteroanterior exposure is made.

With the patient in the same position the tube is aligned vertically and centered over the patient's eye for the lateral view (fig 4). The cassette is placed in the horizontal tunnel, under the

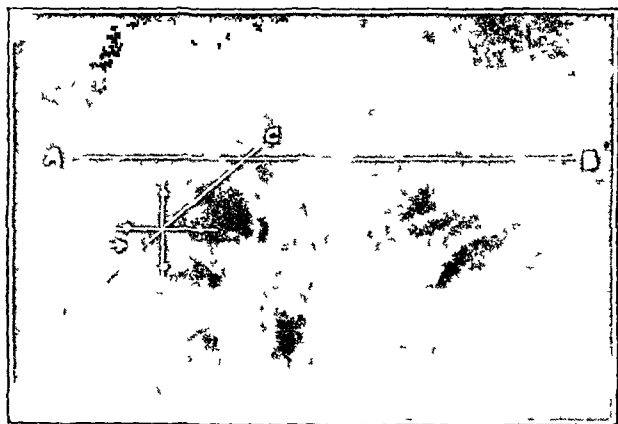


Fig 5—Roentgenogram of an intraorbital foreign body, posteroanterior view, with lines drawn as described in the text. The long diagonal line  $CD$ , which passes through the center of the lens and the foreign body, indicates the meridian in which the body lies. The meridian is determined with the aid of line  $AB$  across the orbits.

patient's head, the position of the contact lens is checked, and the second exposure is made. The patient is then permitted to sit in a chair while the films are developed. If they are satisfactory, the lens is removed. This is done easily by inserting a blunt hook or a tooth stick applicator under the lower edge of the lens while the patient looks up. A special rubber sucker may be used for inserting and removing the lens.

For the localization of a foreign body in the left eye the device is placed at the other end of the table, the patient lies on his left side and the procedure just described is followed.

Stereoscopic films of the head in the lateral or Caldwell position may be made to determine the presence of a foreign body before localization is undertaken. Cassettes with fine grain screens are used, and the exposures are made slightly less dense than for sinuses.

#### METHOD OF PLOTTING THE POSITION OF THE FOREIGN BODY

The film of the posteroanterior view is placed in the viewing box, and a horizontal line is drawn or scratched across the orbits several

millimeters below the upper margins (fig 5, line  $AB$ ). A horizontal and a vertical line are scratched through the shadows of the markers on the contact lens to locate its center. A longer line ( $CD$ ) is then drawn to bisect the foreign body and pass through the center of the lens. The angle formed by this line ( $CD$ ) with the horizontal line through the upper part of the orbit ( $AB$ ) is measured with a protractor and a corresponding line ( $C'D'$ ) at this angle is plotted on a chart representing the front view of the eye (fig 7). Then with a compass and millimeter rule, the distance of the foreign particle from the center of the contact glass is measured. This measurement minus a correction for the magnification of the lens on the film is transferred to the chart. The corrected measurement represents the distance of the foreign body from the anteroposterior axis of the eyeball. The size of the correction factor depends on several variables in the technic. The contact lens is 20 mm in diameter, but on the film it may measure 22 mm. The error then is one tenth of the distance measured on the film. The actual dis-

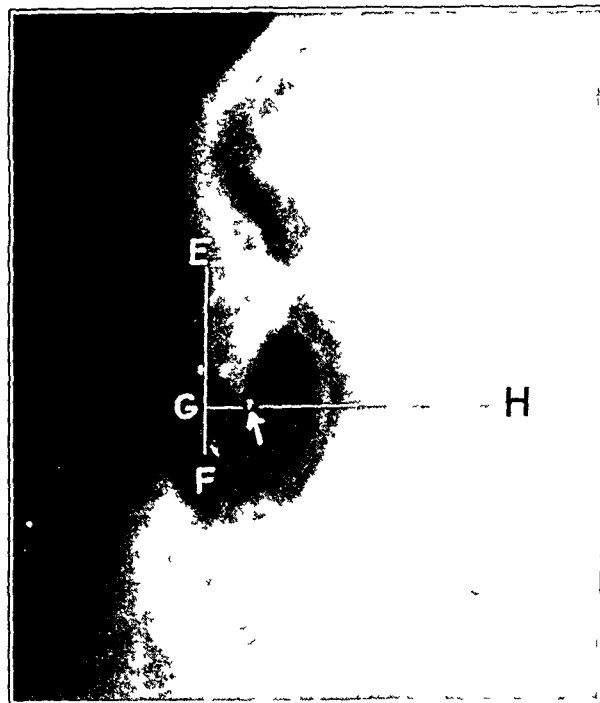


Fig 6—Lateral view of an intraocular foreign body, with a line drawn anterior to the markers to indicate the plane of the limbus ( $EF$ ).  $GH$  is drawn vertical to  $EF$  and through the foreign body, which is indicated by an arrow.

tance of the foreign body from the axis of the eyeball ( $X$ ) may be derived from the equation

Actual diameter of contact glass  $\div$  Diameter of contact glass on the film  $\times$  distance of foreign body from axis of eyeball on the film

In placing the posteroanterior roentgenogram in the viewing box for measuring, care should

be taken to see that it is viewed as an antero-posterior picture, that is, with the right orbit on the left side, as though the patient were being examined directly. The nasal or the temporal side of the eye should be carefully labeled on the chart of the front view (fig 7). This information facilitates interpretation by the surgeon.

The film showing the lateral view (fig 6) is then placed in the viewing box and a line ( $EF$ ) is drawn across the shadow of the contact lens, anterior and tangential to the markers of the

from the axis of the eyeball, which was determined previously. The point at which the two lines cross marks the position of the foreign body in a section of the eyeball at the meridian indicated in the chart of the front view. The charts are made three times the normal size of the eye to increase the accuracy in plotting.

#### SOURCES OF ERROR

The method of localizing intraocular foreign bodies by the use of a contact lens is probably

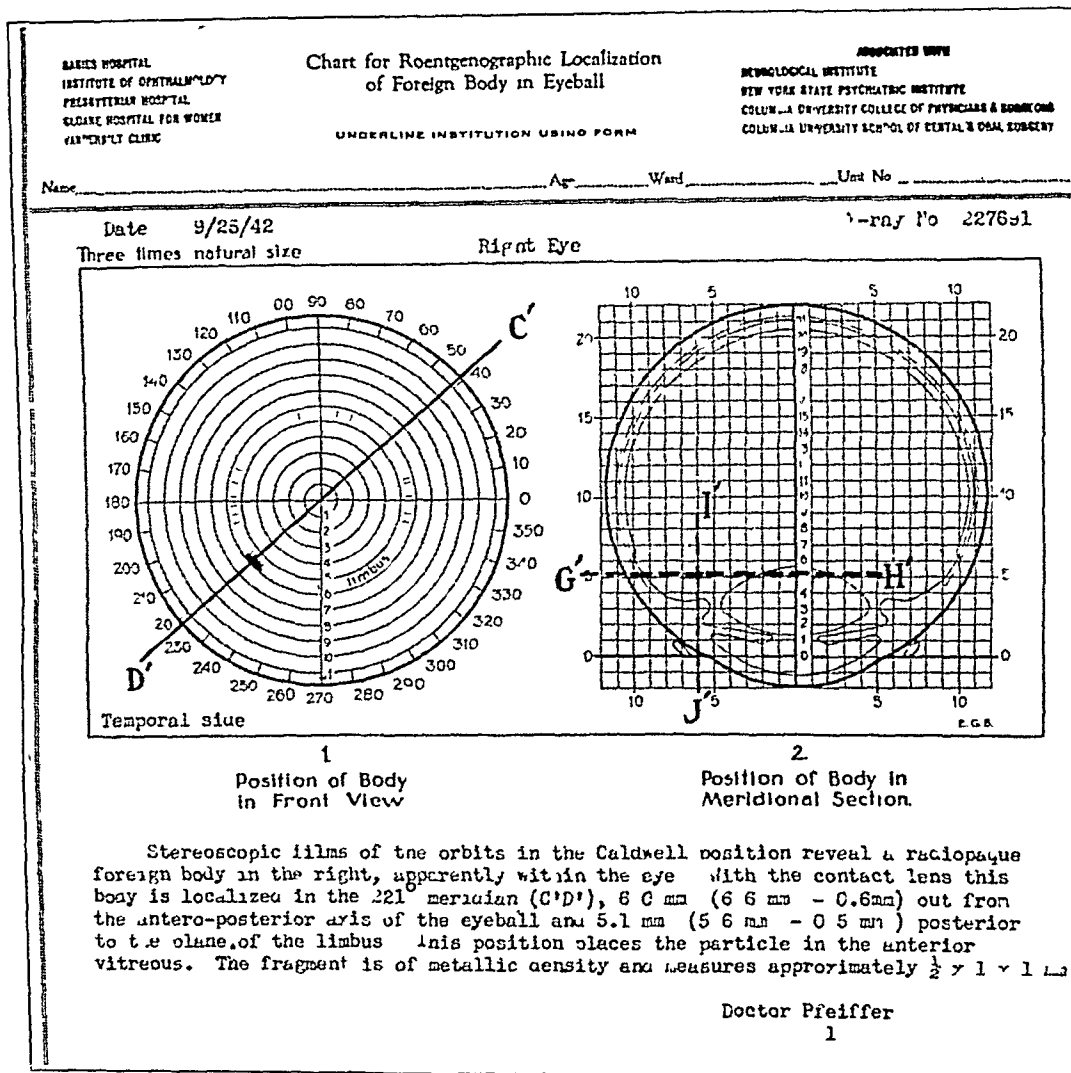


Fig 7—Form on which the location of a foreign body is recorded, including the diagnostic report and charts showing the position of the foreign body as seen in a front view and in a meridional section. In the meridional section the position of the body is at the point at which lines  $I'J'$  and  $G'H'$  cross.

lens, to locate the limbus of the cornea. A second line ( $GH$ ) is drawn perpendicular to the first through the foreign body. A measurement is then taken along the second line from the foreign body to the plane of the limbus. This measurement corrected for magnification represents the actual distance of the foreign body posterior to the plane of the limbus. The location is then plotted on a chart representing a meridional section of the eyeball. A line ( $G'H'$ ) is drawn across the chart parallel with the limbus at the depth calculated. A second line ( $I'J'$ ) is drawn perpendicular to the first to represent the distance of the foreign body

the most accurate technic, for the markers in relation to which the foreign particle is localized rest directly on the eyeball and accurately indicate the position of the eye. Accuracy is gained too by using the plane of the limbus rather than the apex of the cornea as the point of reference in plotting the position of the foreign body. The two films reveal all the information needed for the plotting, and it is scarcely possible to make a significant error. From the roentgenograms one can tell whether the procedure was performed correctly. Chance superimposition of the foreign particle and a marker of the contact lens in the posteroanterior roentgenogram is not

misleading, for the relationship is revealed in the lateral views. Objections to the use of screens scarcely apply to the present day fine grain screens, which give excellent detail. Nothing is to be gained by using film holders.

There is, however, one source of error that may prove disconcerting. It is apparent that one contact lens will not fit all eyes, since eyeballs vary greatly in size and curvature. A lens of average size is used, and fair fitting is usually attained. Frequently there is a tendency for the lens to gravitate downward and thus to leave the curves of the cornea and the sclera. If this happens, the degree of slipping should be estimated and allowed for. The lens may be held in position, however, with the rubber end of a pencil or with a piece of thread the end of which is affixed to the lens with scotch tape.

If a vertical Bucky diaphragm is available the method of exposing the films may be altered so that the patient sits in front of the diaphragm. The technic suggested by Comberg<sup>3</sup> may be followed, and the possible slipping of the lens obviated.

The pencil of primary rays should pass through the eyeball and be perpendicular to the film. Care should be exercised in orienting the tube for the exposures. The patient's head should be placed accurately on the L-shaped device, with the chin against the vertical tunnel and the forehead approximately 2 inches (5 cm) away from it, to approximate the Caldwell position (note the position of the orbital structures on the posteroanterior roentgenogram fig 5). The patient should be carefully instructed to gaze directly forward and not to move the eyes or the head during the exposures.

The measurements used in plotting the position of the foreign body should be determined with a compass from lines accurately scratched

on the films, and the meridian in which the body lies should be determined with a transparent protractor.

#### CONCLUSION

Roentgenographic localization of radiopaque intraocular foreign bodies with the aid of the contact glass of Comberg is accurate, simple, easy to perform, adaptable and requires a minimum of apparatus. A meridional graph of the location, derived from the roentgenograms, is achieved. Bone-free roentgenograms of every patient suspected of having an intraocular foreign body are recommended. The injection of air into Tenon's capsule is helpful in localizing deeply embedded foreign bodies.

635 West One Hundred and Sixty-Fifth Street

#### DISCUSSION

DR A. RUSSELL SHERMAN, Newark, N. J.  
I should like to report an additional aid in the extraction of foreign bodies that have been localized by Dr. Pfeiffer's method. Guist devised a ring to determine the external site of approach to a retinal tear in detachment of the retina. The ring, which is marked at 10 degree intervals, rests on the limbus. A soft metal arm is held at the center of the ring by a thumb-screw and can be revolved like a clock hand so that it points along any desired meridian of the cornea, as indicated by the markings on the ring. Before the ring is applied, the arm is cut to the right length so that its free end will lie over the intraocular foreign body. The ring can be left in position until the sclera is exposed, or it can be reapplied afterward, so that the sclera can be marked directly over the foreign body. I have used this ring in removing 4 intraocular foreign bodies localized by the use of a contact lens. In each instance the foreign body was found directly under the external mark on the sclera.

# CLASSIFICATION OF THE ARTERIOSCLEROTIC-HYPERTENSIVE FUNDUS OCULI IN PATIENTS TREATED WITH SYMPATHECTOMY

LIEUTENANT JEROME A GANS

MEDICAL CORPS, ARMY OF THE UNITED STATES

Considerable impetus was given to the study of hypertension when Goldblatt<sup>1</sup> showed that persistent hypertension could be produced experimentally in dogs by partial clamping of the renal artery. The years that followed brought an extensive literature, based on a renal origin of hypertension. Page<sup>2</sup> showed that persistent hypertension could also be induced by enclosing the kidney in a sac of cellophane, which produced a constricting capsule of scar tissue. The "ischemic" kidney was shown to contain increased amounts of a substance, renin,<sup>3</sup> which combined in the circulation with a renin activator to produce angiotonin, a pressor substance.<sup>4</sup> Then it was found that normal kidney tissue contained an antipressor substance that inactivated angiotonin, this was used by Page and associates<sup>5</sup> to treat hypertensive patients and experimental animals. Thus, various humoral factors and antifactors have come to light.

A different point of view was presented when Heymans<sup>6</sup> showed that persistent hypertension

could be produced neurologically by bilateral excision of the carotid sinus and bilateral section of the cardioinhibitor fibers of the vagus nerve. Reinvestigation of the cold pressor and psychopressor responses has emphasized the nervous mechanisms in hypertension, more particularly since sympathectomy was introduced as therapy. An endocrine basis for hypertension has also been the subject of investigation, especially with respect to the pituitary, thyroid and adrenals, but study along these lines has not been fruitful as yet.

There has been uniform agreement among most investigators concerning the prime importance of the ocular fundus in hypertension, and, accordingly, its status has figured prominently in most studies. From time to time, however, the objection arose that the ocular fundus does not necessarily mirror the condition in other vascular beds of the body. Indeed, there is no evidence that spastic and sclerotic processes in different vascular beds of the body must always keep pace with one another. Another shortcoming may have been the failure to recognize the features of the fundus picture that were pertinent and to separate them from those of lesser significance. More critical examination of the intricate details of the fundus, together with recognition that changes in the fundus arise in the wake of systemic disease, and may at times lag somewhat behind them, has reestablished a major role for the ophthalmoscopic picture. As a result, most clinical classifications of hypertension depend more on the appearance of the eyegrounds than on any other single criterion.

## CLINICAL MATERIAL

The cases reported here cover an investigation that was begun several years ago, in cooperation with studies by Dr Keith S. Grimson, now of Duke University, and Dr Alf S. Alving, Dr Wright Adams and others of the University of Chicago, to determine the relative values of subtotal and of total paravertebral sympathectomy in the treatment of hypertension. The operations of this series were done by Dr Grimson and his associates at the Albert Merritt Billings Hospital, and the technic and surgical results have been separately

From the Division of Ophthalmology, Department of Surgery of the University of Chicago

Read at a meeting of the Chicago Ophthalmological Society, March 15, 1943

1 Goldblatt, H., Lynch, J., Hanzal, R. F., and Summerville, W. W. Studies on Experimental Hypertension, *J. Exper. Med.* **59** 347, 1934. Goldblatt, H. Studies on Experimental Hypertension, *Am. J. Clin. Path.* **10** 40, 1940.

2 Page, I. H. A Method for Producing Persistent Hypertension by Cellophane, *Science* **89** 273, 1939.

3 Harrison, T. R., Blalock, A., and Mason, M. F. Effects on Blood Pressure of Injection of Kidney Extracts of Dogs with Renal Hypertension, *Proc. Soc. Exper. Biol. & Med.* **35** 38, 1936.

4 Page, I. H. The Vasoconstrictor Action of Plasma from Hypertensive Patients and Dogs, *J. Exper. Med.* **72** 301, 1940. Page, I. H., and Helmer, O. M. A Crystalline Pressor Substance (Angiotonin) Resulting from the Reaction Between Renin and Renin-activator, *ibid.* **71** 29, 1940.

5 Page, I. H., Helmer, O. M., Kohlstaedt, H. K., Kempf, G. F., Corcoran, A. C., and Taylor, R. D. A Progress Report of Investigations Concerned with the Experimental Treatment of Hypertension with Kidney Extracts, *Ann. Int. Med.* **18** 29-41, 1943.

6 Heymans, C. Some Aspects of Blood Pressure Regulation and Experimental Arterial Hypertension, *Surgery* **4** 487, 1938.



reported by him<sup>7</sup> Other sympathectomies performed since the original series will not be considered here The full operative procedure required two transthoracic and one transabdominal operation The stellate ganglion and the entire thoracic sympathetic ganglionated chain, the splanchnic nerve and its branches, the major portion of the celiac ganglion and part, or all, of the lumbar sympathetic ganglionated chain were removed In some cases the abdominal operation was omitted In all the patients a typical Horner syndrome developed bilaterally, with varying degrees of ptosis and miosis, although enophthalmos was irregular and slight In several there developed changes in reading tolerance sufficient to merit note, but, unfortunately, preoperative and postoperative studies of accommodation were not undertaken Postoperative sweating tests contributed further proof of the absence of sympathetic function in the affected areas

The observational routine before and after sympathectomy included determinations of the blood pressure every four hours under basal conditions, as well as after immersion of the hands in ice water and with the

visual fields, refraction and such other studies as were deemed advisable

The series contained 18 hypertensive patients, 10 of whom were males and 8 females The ages ranged from 18 to 50 at the time of operation, with an average age of 35.8 years Four patients were in Keith-Wagener<sup>8</sup> group I (mild hypertension), 4 in group II (moderate hypertension), 4, in group III (advanced hypertension), and 6, in group IV (very severe hypertension) Six patients had had cerebral hemorrhage with hemiplegia before operation, and 2 others had had severe episodes of hypertensive encephalopathy There were 3 operative deaths in the series, 1 of a patient in Keith-Wagener group III and 2 of patients in group IV Two deaths were due to sudden respiratory failure on the second and the fifth postoperative day respectively, the other death was the result of late pneumonia and uremia Three other patients, tabulated as surviving operation, have died since One lived for two and one-quarter years after the third stage of hypertension and died of cardiac failure, renal insufficiency and intestinal volvulus Two others died at home, and

TABLE 1—Effect of Subtotal to Total Sympathectomy on Blood Pressure\*

Keith Wagener Group	Age of Patient, Yr	Preoperative Blood Pressure		Postoperative Blood Pressure						Time in Months	
		Supine Position		Supine Position			Standing				
		O	P D †	Hospital	O	P	D	Hospital	O		P
I	25	190	116	166/100	130/	84	108/	70	120/	70	24
I	38	210	138	180/120	126	128	174	108	162	120	22
I	32	200	126	170/118	110/	75	120/	80	70/	50	7
I	27	180	108	180/110	152	100	140/	94	90/	60	5
II †	42	224	120	200/120	200	108	130/	94	138/	92	24
II †	40	196	120	180/116	170	104	138/	88	122/	90	18
II	18	204	140	190/130	128/	74	126/	86	114/	76	17
II	25	180	126	160/118	120/	72	116/	76	116/	70	7
III	40	264	136	220/122	246	138	200	114	180	100	21
III	33	240	150	228/138	260	150	200	142	196	120	20
III	44	220	124	170/120	196	122	160	100	122/	90	15
IV †	50	278	148	220/130	234	130	172	102	152	118	21
IV †	42	238	154	202/132	240	140	210	134	180	130	9
IV	40	280	138	226/150	220	142	182	120	184	132	8
IV †	28	228	130	178/120	140/	86	138/	88	100/	76	7

\* After Grimson<sup>7b</sup>  
† O P D indicates an average for several office readings  
‡ Cerebral accident before operation

patient under profound hypnosis induced with sodium amytal Renal studies undertaken by Dr Alving, of the department of medicine of the University of Chicago, included a urea clearance test, the Addis-Shevky urine concentration test, the taking of intravenous pyelograms and determinations of inulin and diodrast clearances Circulatory tests, made by Dr Wright Adams, included a roentgenographic study of the chest, an electrocardiographic reading, determinations of the arm to tongue circulation time and the venous pressure, estimations of blood volume and vital capacity, determination of cardiac output and exercise tolerance tests Neurologic and psychiatric evaluations were also obtained Ophthalmologically, an attempt was made to photograph each fundus before and after operation and to describe each fundus in detail before operation, with comments later concerning any changes observed in the posterior course These examinations were supplemented by examination of the

no autopsy was performed The rest have survived for periods of from one and a quarter to three years There was definite symptomatic improvement Table 1, from Grimson's recent review,<sup>7b</sup> shows the effect on the blood pressure Adams, Alving and associates<sup>9</sup> issued a preliminary report covering only the first seven months after operation They found no significant consistent change in insulin or diodrast clearance, urine concentration ability, venous pressure, arm to tongue circulation time or size of the heart, either in the patients who did or in those who did not obtain good reduction in blood pressure None of the circulatory changes found account for the drop in blood pressure when it occurred They concluded that it seemed probable that the drop in pressure that occurs after sympathectomy is due to decrease in peripheral resistance in a large vascular bed

8 Keith, N M, Wagener, H P, and Barker, N W Some Different Types of Essential Hypertension Their Course and Prognosis, *Am J M Sc* **197** 332, 1939

9 Adams, W, Alving, A S, Sandiford, L, Grimson, K S, and Scott, C The Effect of Bilateral Paravertebral Sympathectomy on the Cardio-Renal System in Essential Hypertension, *Am J Physiol* **133** 190-191 (June) 1941

7 (a) Grimson, K S Total Thoracic and Partial to Total Lumbar Sympathectomy and Celiac Ganglionectomy in the Treatment of Hypertension, *Ann Surg* **114** 753, 1941, (b) The Surgical Treatment of Hypertension, *Internat Abstr Surg* **75** 421-434, 1942, in *Surg, Gynec & Obst* November 1942

## PREREQUISITES FOR CLASSIFICATION

It was difficult to review cases from an ophthalmologic standpoint with the Keith-Wagener classification. While it is recognized that this classification is effective in evaluating the condition of the hypertensive patient as a whole, certain difficulties arise when it is used with reference to the eye. For example, groups I and II of Keith and Wagener frequently present such similar fundus pictures that they are well nigh indistinguishable on the basis of the eyes alone. Peet and associates<sup>10</sup> recognized this in 1940, when they proposed their own classification to assist them in their studies. Fishberg's<sup>11</sup> classification of hypertensive neuroretinopathy, arteriosclerotic retinopathy and choked disk was helpful, but permitted no designation of degree within each group. Nor did it allow cross classification of changes in the fundus that were both hypertensive and sclerotic. The classification of vascular fundus disease originated by Gifford and MacPherson<sup>12</sup> was found to be better suited to the ophthalmologic aspects of this study than any of the others, but, unfortunately, it was impossible with this classification to evaluate the sclerotic components of the fundus apart from the hypertensive components. Since in such a study as this it was of interest to classify separately the sclerotic, organic disease of the vessels and the functional, acute hypertensive component, a classification that permitted this was necessary.

To classify the fundus accurately there must be agreement on certain axiomatic principles. The interpretations of spasm, light reflex, preorganic constriction, organic constriction, irregularity of lumen and arteriovenous nicking are so basic as to demand early consideration. It is well recognized that it is the blood column, not the vessel, which is seen in the normal fundus.<sup>13</sup> This is due to the transparency of the wall of the normal vessel. Only at and near the disk, where the vessel wall is thicker and less transparent, is the wall itself visible, appearing as a grayish sheathing on the blood column. The light reflex on the vessel is a combination of the

reflex from the vessel wall (mainly at the adventitia-media interface) and the reflex from the blood column.<sup>14</sup>

A consideration of the light reflex from the penholder in figure 1 *a* is illustrative. The width of the light reflex is proportional to the diameter of the reflecting surface, that is, wherever the penholder is wide, the reflex is wide, where the diameter narrows, the reflex narrows. The same relation holds true for the vessels of the fundus, large vessels have wide reflexes, and smaller ones have narrower reflexes. The principle is also true in another respect. Let figure 1 *b* represent a normal artery in cross section

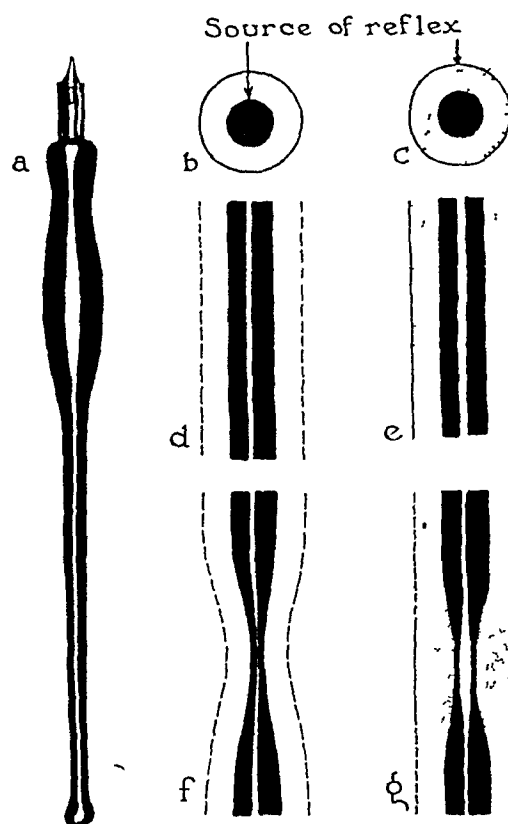


Fig 1—Variations in the light reflex (see text for details)

Although the arterial media is appreciable and contributes slightly to the reflex, the main source of the reflex is the surface of the blood column, seen ophthalmoscopically, as in figure 1 *d*. If the arterial media is thickened, hyalinized or made optically more dense by a sclerosing process, it takes on major importance as the source of the reflex, as shown in figure 1 *c*, and as seen ophthalmoscopically in figure 1 *e*. This principle is also applicable to a comparison of the normal vein and the normal artery. In the former the media is negligible, and all the reflex comes from the blood column, whereas in the latter there is sufficient media to produce some widening of the reflex. Thus, arteries normally

10 Peet, M. M., Woods, W. W., and Braden, S. The Surgical Treatment of Hypertension. Results in 350 Consecutive Cases Treated by Bilateral Suprarenal Splanchnicectomy and Lower Dorsal Sympathetic Ganglionectomy, *J. A. M. A.* **115**: 1875-1885 (Nov. 30) 1940.

11 Fishberg, A. M. Hypertension and Nephritis, ed. 4, Philadelphia, Lea & Febiger, 1939.

12 Gifford, S. R., and MacPherson, W. A. A Classification of Vascular Fundus Diseases, *Quart. Bull. Northwestern Univ. M. School* **14**: 65, 1940.

13 Duke-Elder, W. S. Textbook of Ophthalmology, London, Henry Kimpton, 1940, vol. 3, p. 2677.

14 Wilmer, W. H., Pierce, H. F., and Friedenwald, J. S. The Light Streaks of the Retinal Blood Vessels, *Arch. Ophth.* **9**: 368 (March) 1933.

have wider reflexes than veins of the same lumen diameter

Figure 1 *f* represents an artery with a wall of normal transparency, physiologically stimulated to contract at a focal area. Since the vessel wall at the constricted area is transparent and the reflex arises mainly from the blood column, the narrowed blood column will give a narrower reflex. This phenomenon of narrowed blood column and narrowed light reflex is the expected picture of a true spasm, or preorganic constriction, indeed, it is the picture found in the early stages of hypertension and in cases of toxemia of pregnancy that arises without previous vascular disease. Figure 1 *g* represents a vessel with an area of considerable medial thickening and intimal proliferation, sufficient to encroach on the vessel lumen. If one judges from the constricted blood column alone, it differs little from the true spasm, shown in figure 1 *f*. But the notably widened reflex indicates that the blood column is not contributing the greater share of the reflex and that the thickened wall is the reflecting surface. Differentiation of preorganic spasm from organic sclerosis in this manner will facilitate classification in most cases, confusion arising only when spasm has existed over a long period and sclerosis has begun to appear. In such cases, other areas of the fundus in the same eye or in the fellow eye may provide the crucial clues.

Another factor in sclerosis is the appearance of vessel sheathing. Mention has already been made of normal sheathing of vessels about the disk, which is due to the increased thickness of the vessel and the greater optical density where the vessels originate. Sclerotic sheathing arises from loss of transparency of the vessel wall, it manifests itself as parallel white or yellowish white lines bordering the red blood column and should be seen at least 1 disk diameter away from the disk to be of significance. Frequently the sclerosis is insufficient to become visible in itself but may still alter the red character of the blood column to produce the familiar copper-red color, or when still more pronounced may, in combination with a wide reflex of increased brilliance, produce characteristic "silver wiring."

Arteriovenous compression and nicking were first described by Gunn<sup>15</sup> in 1892. Although Gunn stated that "the appearance is interpreted

as an evidence of high arterial tension," more recently Friedenwald<sup>16</sup> suggested

[Whereas these] cases usually present marked arterial hypertension, the constriction of the veins persists when, as the result of intercurrent disease or cardiac decompensation, the blood pressure falls to normal levels. The constriction is to be attributed, therefore, not to the hypertension directly, but to structural changes in the vessel wall.

Koyanagi's<sup>17</sup> observation of sclerotic changes, which convert the common adventitial sheath about the vein and artery at crossing sites into a constricting band, adds weight to this interpretation. Although venous thromboses at the sites of nicking are common, few authors have considered them of sufficient importance to merit a separate position in the classification of arteriosclerotic disease. But since nicking is understood to be a sclerotic phenomenon, and since severe nicking predisposes to venous occlusion at the site of the compression, such thromboses should be considered evidence of an extreme degree of sclerosis. One must tread this ground cautiously, for not all thromboses are the result of sclerotic compression, nor are all arterial closures sclerotic. But if one bars such irrelevant vascular disease as embolism and focal perivasculitis (tuberculous or otherwise) and causes other than arteriosclerotic-hypertensive disease, these focal vascular insufficiencies do indicate a most severe degree of sclerosis.

Finally come those factors of the fundus picture related not to sclerosis but to acute hypertensive "toxicity." The subtle changes of early disease have been best observed during acute hypertensive episodes without previous vascular disease, such as the toxemia of pregnancy<sup>18</sup>. The early development of edema of nerve fibers, which blurs the margins of the disk and frequently extends out into the retina above and below, has been widely noted, although the exact mechanism of the neurotoxicity has not been elucidated. That this is a reversible change has been repeatedly confirmed by observations of regression to the normal state after toxemia has ended. This type of neural edema is not to be confused with the frank papilledema seen in the late stages of malignant hypertension. In the latter condition the disk is measurably mushroomed forward, and there is increased intracranial pressure, whereas in the former the disk

15 Gunn, R. M. Ophthalmoscopic Evidence of (1) Arterial Changes Associated with Chronic Renal Disease, and (2) of Increased Arterial Tension, *Tr. Ophth. Soc. U. Kingdom* 12:124, 1892.

16 Friedenwald, H. The Doyne Memorial Lecture: Pathological Changes in the Retinal Blood Vessels in Arteriosclerosis and Hypertension, *Tr. Ophth. Soc. U. Kingdom* 50:452, 1930.

17 Koyanagi, Y. Die Bedeutung der Gefasskreuzung für die Entstehung der Asthrombose der retinalen Zentralvene, *Klin. Monatsbl. f. Augenh.* 80:219, 1928.

18 Dieckmann, W. J. The Toxemias of Pregnancy, St. Louis, C. V. Mosby Company, 1941, chap. 8.

is flat, though fuzzy and wet, and the intracranial pressure is unaltered. Preorganic arterial spasm, another early sign that may parallel neural edema, has been discussed from its anatomic and ophthalmoscopic standpoint. Although the cause is obscure, it has been seen that spasms may relax and disappear,<sup>19</sup> or when they persist for a long time, they may go on to hyaline degeneration and sclerosis.

Although neural edema and spasm are early phenomena, this cannot be said about the flame-shaped hemorrhages and soft exudates seen in cases of hypertensive disease. With toxemia of pregnancy they are seen at a much later stage and must be interpreted as a beginning breakdown in the integrity of the vessel, sufficient to allow escape of fluid and formed elements of the blood. The form which the lesions take and their course and outcome are modified by degenerative changes and by invasion of phagocytes.

The superimposition of choked disk, with true elevation of the nerve head, is generally considered the final, most severe, stage, i. e., malignant hypertension. The papilledema arises not by local vascular processes, as in the case of neural edema, hemorrhage and exudate, but in the fashion of the papilledema of cerebral tumor, from increased intracranial pressure.

#### CLASSIFICATION

With these factors in mind, the classification in table 2 was devised. The arteriosclerotic and the acute factors are evaluated separately and classified as of four grades, according to the following criteria. If there is beginning disease of the vessel, such as slightly widened reflex, early crossing signs or sheathing or irregularity of the lumen, the condition is designated as grade  $A_1$ . Patients with this stage of the disease may have slight derangement of pigment at the macula but no visual defect. If there is advanced vascular disease, with notable widening of the reflex stripe or severe arteriovenous deviation or nicking, the condition is classified as grade  $A_2$ . At this stage there may be hard, shiny exudates. If, in addition to changes characteristic of grade  $A_2$ , there are signs of a focal vascular insufficiency, such as venous thrombosis, or other vascular occlusions, the designation is grade  $A_3$ . An old thrombosis may show a field defect only. Perhaps certain other conditions, such as macular lesions on a vascular basis, may actually belong to this type but for the present they are excluded from con-

sideration. Absence of any organic changes places such a fundus in the  $A_0$ , or normal group. The hypertensive classifications are straightforward. Focal arteriolar spasm or mild edema of the nerve fibers of the disk or retina is classified as grade  $H_1$ . Hemorrhages or soft exudates are classified as grade  $H_2$ . If papilledema has supervened, the designation is grade  $H_3$ .<sup>20</sup> Again, absence of any acute signs places such a fundus in the  $H_0$ , or normal, group. Each patient is classified according to both the A and the H groupings. Thus, a patient's classification may be  $H_1$  and yet  $A_3$  or  $A_1$  and  $H_3$ . In

TABLE 2—Classification of Vascular Disease of the Fundus

A <sub>0</sub> H <sub>0</sub> —Normal	
A <sub>1</sub> Mild arteriolar sclerosis	H <sub>1</sub> Arteriolar constriction
A <sub>2</sub> Severe arteriolar sclerosis	H <sub>2</sub> Hypertensive retinopathy
A <sub>3</sub> Severe arteriolar sclerosis with focal insufficiency	H <sub>3</sub> Hypertensive retinopathy with papilledema

this fashion, a separate evaluation is made of organic vascular sclerosis and preorganic acute toxicity.

#### RESULTS OF SYMPATHECTOMY

Table 3 summarizes the changes in the fundus in each of the patients and, at the same time, gives some of the pertinent clinical information. The designations for postoperative blood pressure that appear in the table constitute a code which facilitates tabulation. The blood pressure readings published by Grimson have been

<sup>20</sup> Alving, in a personal communication, suggested that the purpose of classification would be better served if  $H_3$  were removed from the H series since papilledema is etiologically different from the other acute signs. He suggested that papilledema be made a third, and separate, factor, as it is in Fishberg's classification. This led to the temporary adoption of a third designation P (for papilledema), with the fundi classified according to the three factors A, H and P. The diopeters of papilledema were expressed in the P subscript, so that  $A_1H_2P_2$  might represent a fundus of mild sclerotic changes with hemorrhages or soft exudates and 2 D of papilledema. However, in many cases of papilledema it is difficult to assess whether hemorrhages and exudates are primarily hypertensive or actually secondary to the choked disk. Also, papilledema produces secondary arterial constriction and venous dilatation, which further confuse the picture. Altogether, papilledema makes evaluation of the other factors so difficult that it is questionable whether separation of a P factor provides greater accuracy. For the sake of simplicity it would seem that papilledema can still be represented in the H series if the difference in pathogenesis of hypertensive hemorrhages and exudates and that of choked disk is kept in mind. Only in cases in which choked disk occurs with vessel spasms and without hemorrhage or exudate would classification be difficult, and such an occurrence is not common.

<sup>19</sup> Haselhorst, G., and Mylius, K. Zur Frage der Gefasskrämpfe bei Eklampsie, Zentralbl. f. Gynak. 52: 1180, 1928.

arranged into four groups I signifies that the postoperative blood pressure was less than 140 systolic and 90 diastolic when the patient was in both the supine and the standing position, II signifies that the blood pressure was less than 140 systolic and 90 diastolic with the patient in the standing position but that it continued to be elevated with the patient lying down III indicates that the blood pressure was appreciably lower after than before operation, but not down to 140 systolic and 90 diastolic, and IV, that the blood pressure was essentially unchanged by operation

TABLE 3—*Appearance of the Fundus in Hypertensive Patients After Sympathectomy*

	Age	Sex	Keith Wagener Classifi- cation	Fundus Picture		Post operative Blood pressure *
				Pre operative	Post operative	
R. B	25	F	I	A <sub>1</sub> H <sub>1</sub>	A <sub>1</sub> H <sub>0</sub>	I
I. M	38	F	I	A <sub>1</sub> H <sub>1</sub>	A <sub>1</sub> H <sub>1</sub>	IV
H. M	31	F	I	A <sub>1</sub> H <sub>1</sub>	A <sub>1</sub> H <sub>1</sub>	I
C. O †	27	M	I	A <sub>0</sub> H <sub>1</sub>	A <sub>1</sub> H <sub>1</sub>	II
H. S	42	M	II ‡	A <sub>1</sub> H <sub>2</sub>	A <sub>1</sub> H <sub>1</sub>	III
E. R	39	M	II ‡	A <sub>1</sub> H <sub>1</sub>	A <sub>1</sub> H <sub>1</sub>	I
J. W	18	F	II	A <sub>0</sub> H <sub>1</sub>	A <sub>1</sub> H <sub>0</sub>	I
J. L	25	F	II	A <sub>0</sub> H <sub>1</sub>	A <sub>1</sub> H <sub>1</sub>	I
L. M	40	F	III	A <sub>2</sub> H <sub>2</sub>	A <sub>3</sub> H <sub>1</sub>	III
A. W	32	F	III	A <sub>2</sub> H <sub>2</sub>	A <sub>2</sub> H <sub>1</sub>	IV §
Mc T	44	M	III	A <sub>1</sub> H <sub>2</sub>	A <sub>1</sub> H <sub>1</sub>	II
G. H	43	M	III	A <sub>3</sub> H <sub>1</sub>	Died	
L. M	50	M	IV †	A <sub>2</sub> H <sub>2</sub>	A <sub>2</sub> H <sub>1</sub>	III
D. Mc	42	M	IV †	A <sub>2</sub> H <sub>3</sub>	A <sub>2</sub> H <sub>1</sub>	IV
P. L	40	M	IV	A <sub>1</sub> H <sub>3</sub>	A <sub>1</sub> H <sub>1</sub>	III
V. M	28	M	IV ‡	A <sub>1</sub> H <sub>3</sub>	A <sub>1</sub> H <sub>1</sub>	I
R. E	48	M	IV	A <sub>2</sub> H <sub>3</sub>	Died	
C. D	32	F	IV ‡	A <sub>2</sub> H <sub>3</sub>	Died	

\* I indicates a blood pressure of less than 140 systolic and 90 diastolic when the patient was in the supine and standing positions, II, a pressure of less than 140 systolic and 90 diastolic when the subject was standing but an elevation of pressure in the supine position, III, a pressure lower than before operation, but not down to 140 systolic and 90 diastolic, and IV, no lowering of blood pressure  
† The patient had polycythaemia vera  
‡ A cerebral hemorrhage occurred before operation  
§ The patient died two and a half years after operation  
|| The patient died at home in the follow up period No autopsy was performed

The cases of certain of the patients were sufficiently representative that they merit individual presentation

R. B., a housewife, was 25 at the time of her operation. She was found to have a blood pressure of 180 systolic and 110 diastolic, with blood and albumin in her urine, during a pregnancy three and one-half years before operation. After a therapeutic abortion her blood pressure rose to 220 systolic and 120 diastolic. While she was under medical management for about two and one-half years, the blood pressure remained about 180 systolic and 110 diastolic. The urine was normal. The fundus showed changes characteristic of grade A<sub>1</sub>H<sub>1</sub>, that is, there were mild sclerotic vascular changes, as well as some spasms. After sympathectomy there was a prompt drop of the blood pressure to and below normal levels. This patient has now been followed over two and one-half years, and on the last admission to the hospital her blood pressure

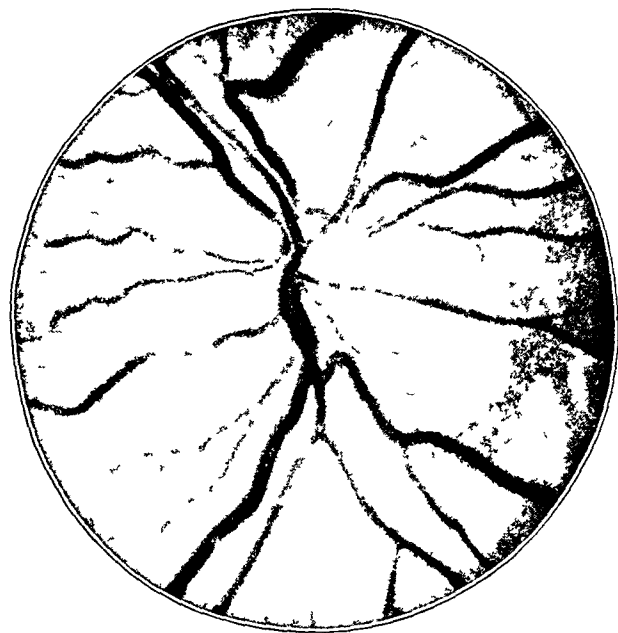


Fig 2—R. B., aged 25 at the time of operation, had had persistently normal blood pressure since operation. The mild degree of focal arteriolar sclerosis (widening of the arteriolar light reflex with narrowing of the lumen of the vessel) is readily noted.

averaged 110 systolic and 65 diastolic. Figure 2 shows the picture of the fundus at the last admission. The old areas of arteriolar sclerosis are in bold contrast to the more normal vasculature in other areas of the fundus. No spasms are visible at present.

Equally good results were obtained in the case of V. M., a laborer aged 28, who was first seen seven weeks after a paralytic stroke. Examination showed a blood pressure of 230 systolic and 150 diastolic and



Fig 3—L. M., aged 40, derived little benefit from sympathectomy. The left fundus reveals that the arteriolar sclerosis is pronounced, the arteriolar light reflex is widened almost throughout and the veins are practically cut into "sausages" by severe nicking. Examination of the right eye showed a field defect due to an old venous thrombosis, and punctate exudate, such as are seen with old thromboses of branch veins in this region of the fundus.

right hemiplegia. The fundus showed some edema of the disk, with edema streaking out into the retina, mild crossing signs and a fresh cotton wool exudate. While the patient was under observation, the edema of the nerve head increased to frank papilledema, and sympathectomy was performed. The blood pressure has been consistently normal with the patient in both the standing and the recumbent position for the past year and a half since operation. Papilledema and exudate have disappeared, although some residual edema of the nerve fibers on the disk remains.

One often learns considerably more from the failures with a procedure than from the successes. The preoperative blood pressure curve in the case of L. M., a 40 year old widow, was about 236 systolic and 128 diastolic. Medical management over the course of a year and eight months produced no beneficial effect. The result of operation also left much to be desired, although there was some initial drop in the blood pressure (180 systolic and 100 diastolic in the recumbent position and 200 systolic and 114 diastolic in the supine position), and the patient claimed she felt better. Figure 3 shows the preoperative appearance of the fundus in the patient. The degree of the organic vascular component was pronounced, although papilledema was absent.

One of the fatalities was G. H., aged 43. He had macular degeneration in the right eye, possibly on a vascular basis, and thrombosis of a branch vein in the left eye. In the fundus the crossing signs were pronounced, the arteriolar sclerosis was severe, and hemorrhages were seen in the area of the venous thrombosis.

Table 4 shows the distribution of fundus groupings before and after operation. The arteriolar sclerosis showed a slight tendency to shift toward the higher grades. In the 3 patients with grade A<sub>0</sub> who showed no sclerosis at first, grade A<sub>1</sub> changes developed. A patient who had grade A<sub>2</sub> signs shifted to grade A<sub>3</sub> signs. Two patients with grade A<sub>2</sub> changes and 1 with grade A<sub>3</sub> changes died. It is difficult to assess such an increase in sclerosis as was observed. The findings in the H series are in direct contrast to those of the A series. After sympathectomy there was a definite shift to the more benign grades of hypertensive disease, the shift occurring in 10 patients. All the papilledema disappeared in the patients who survived (2 patients with papilledema died after operation). In all the patients with grade H<sub>2</sub> changes hemorrhage and exudate were absorbed, the picture shifting to grade H<sub>1</sub>. It appears significant that all hypertensive changes did not disappear entirely. In 13 of the 15 patients who survived, evidence of spasm remained, as well as some edema of nerve fibers, even though the disk was not measurably elevated.

In table 5 the fundus picture correlated with the postoperative blood pressures. There is a notable correlation between the degree of sclerosis and the prognosis of the patient in so far as both the drop in blood pressure and the out-

look for survival are concerned. The patients with the least sclerosis achieved normal blood pressures, while those with the most severe sclerosis obtained the least decrease in blood pressure. It was also found that the mortality was limited exclusively to the patients with the greatest degree of sclerosis. Whereas there was a high degree of correlation in the A series, the H series presented a somewhat different pic-

TABLE 4—Distribution of Fundus Types

Classification of Fundus	Number of Patients	
	Preoperative	Postoperative
A <sub>0</sub>	3	0
A <sub>1</sub>	8	11
A <sub>2</sub>	6 (2 died)	3
A <sub>3</sub>	1 (1 died)	1
	18 (3 died)	15
H <sub>0</sub>	0	2
H <sub>1</sub>	8 (1 died)	13
H <sub>2</sub>	5	0
H <sub>3</sub>	5 (2 died)	0
	18 (3 died)	15

TABLE 5—Relation of Fundus Picture to Effect of Sympathectomy on Blood Pressure and Mortality Rate

Classification of Fundus	Effect on Blood Pressure *				Number of Deaths
	I	II	III	IV	
A <sub>0</sub>	1	1			
A <sub>1</sub>	4	1	2	1	
A <sub>2</sub>			2	2	2
A <sub>3</sub>					1
H <sub>0</sub>					
H <sub>1</sub>	5	1		1	1
H <sub>2</sub>		1	3	1	
H <sub>3</sub>	1		1	1	2

\* The grading of blood pressure is the same as that in table 2.

TABLE 6—Relation of Fundus Picture to Decrease in Diastolic Pressure and Mortality Rate

Classification of Fundus	Diastolic Pressure Decrease, Mm					Increase	Deaths
	40-49	30-39	20-29	10-19	0-9		
A <sub>0</sub>	2			1			
A <sub>1</sub>		3	4	1			
A <sub>2</sub>			1		1	2	2
A <sub>3</sub>							1
H <sub>0</sub>							
H <sub>1</sub>	2	2	1	2			1
H <sub>2</sub>			3		1	1	
H <sub>3</sub>		2	-			1	2

ture. Although a general trend suggests a better prognosis for patients with the least morbid changes, there is more scatter than in the A series, and the correlation appears to be less rigid. Correlation of the fundus picture with the numerical drop in diastolic blood pressure (table 6) rather than arbitrary grouping reveals the same tendencies, although not to such a striking degree. Patients with the lesser degrees of sclerosis, again, showed a more consistent



diop in diastolic pressure, and those with greater degrees of sclerosis showed the least fall in diastolic pressure. In the H series, the same trend is suggested, but the scatter is greater and the correlation less valid. In table 7 the age of the patient is correlated with the postoperative blood pressure. Despite considerable scatter, there is the suggestion that the best results occur in the youngest patients and the poorest results in the oldest patients.

COMMENT

The study has revealed certain trends, and, within the limits of error that are imposed by the small series, it is justifiable to make certain observations. First, coincident with a fall in the systolic and diastolic blood pressures in many cases, the acute signs in the fundus disappeared

tuire. Heretofore, the prognosis for a patient has always been measured in terms of the acute hypertensive signs, namely, hemorrhage, exudate and papilledema, possibly because these signs were the most easily and unmistakably noted. The prognostic value of these signs has led to their being used as a basis of classification practically universally. From this study, however, it appears that the acute hypertensive signs are actually of less prognostic value than the sclerotic signs, in so far as benefit from operation is concerned. This is not at all startling, since the acute hypertensive signs are all reversible and may disappear without trace, whereas the degree of sclerosis is for the most part irreversible. Further evidence in this regard arises from a consideration of the main theories that have been suggested concerning the mechanism of sympathectomy. Crile<sup>21</sup> suggested that denervation of the adrenal medulla was a major factor. Other authors have at various times suggested that the effect was produced by such factors as dilation of renal vessels, dilation of the cardiac vessel bed and dilation of the splanchnic bed. Except for the neurologic concept of Crile, all the other theories depend on the ability of an arterial bed to dilate. Rigidity of this bed, i. e., sclerosis, would be an insurmountable obstacle to dilation and should be the main limiting factor in the achievement of a good result. Page and associates reported that patients suffering from the malignant syndrome showed reversal of the morbid changes in the eyegrounds after administration of renal extract.<sup>5</sup> But his published clinical charts show that the morbid changes which regressed were the hemorrhages, papilledema and exudates, while the sclerotic changes in the vessels appeared to remain fixed, or even progressed. It would be interesting to learn whether the degree of sclerosis has any relation to the success or failure of administration of renal extract.

If, then, the degree of sclerosis is the basic factor in evaluating prognosis with respect to surgical treatment, any factor that affects the degree of sclerosis should secondarily be of prognostic value. It is possibly for this reason that age is of prognostic value, since in younger persons sclerosis has not had sufficient time to develop. Or, perhaps, duration of the disease, if it could be accurately known, might have the same prognostic value, since it will affect the degree of sclerosis. Finally, perhaps the degree of the acute hypertensive component, which is still emphasized so greatly, is really of value only in so far as it affects the organic sclerosis.

21 Crile, G. The Surgical Treatment of Hypertension, Philadelphia, W. B. Saunders Company, 1938.

TABLE 7—Relation of Age to Effects on Blood Pressure and Mortality Rate

Age	Effect on Blood Pressure *				Died
	I	II	III	IV	
25	3				
26-30	1	1			
31-35	1			1	1
36-40	1		1	1	
41-45		1	1	1	1
46-50			1		1

\* The grading of blood pressures is the same as that in table 2.

after sympathectomy. Papilledema, hemorrhages and exudates were all noted to disappear, although it is significant that some residual edema of nerve fibers about the disk and some vessel spasms persisted in a large majority of patients. Thus, the eyegrounds tend to confirm the beneficial effects that have been found to follow sympathectomy.

The persistence of some degree of signs of "toxic hypertension" in the fundus, such as spasm and neural edema, even after sympathectomy, which denervates the sympathetic supply to the ocular vessels, must be regarded as highly significant. In cases of toxemia of pregnancy in which such signs are noted, they start to disappear almost immediately after delivery of the baby, and in the course of several days (rarely more than a few weeks) they are completely gone. If the neural edema and spasm that persisted in the large majority of the patients are indicative of continuing vascular disease, as indeed they appear to be, one would be forced to the conclusion that sympathectomy has not completely arrested the disease process, even though it has provided relief in many instances from the elevated blood pressure.

Another impression that appears justifiable concerns the prognostic value of the fundus pic-

These suggestions are in keeping with the statement of Woods and Peet<sup>22</sup> that a favorable prognosis seems to depend on the degree of retinal arteriolar sclerosis rather than on the level of the blood pressure, the absence of retinitis with hemorrhage and exudate or papilledema. This well emphasizes the need for a classification that will give the proper evaluation to the arteriolar sclerosis. Such a classification, tentative though it may be, has been suggested. Experience may dictate further revision in this respect.

#### SUMMARY

Eighteen patients of all ages, and with all stages of hypertension, were subjected to total or subtotal paravertebral sympathectomy of the most extensive type yet reported, and of particular note in that the retinal vessels were also denervated by stellate ganglionectomy. In the 15 patients who survived operation, varying degrees of lowering of blood pressure were obtained. In order to secure separate evaluation of arteriolar sclerosis and the acute hypertensive changes in the fundi, a double classification was devised. In the arteriosclerotic division,  $A_0$  represented no sclerotic changes in the fundi. Minimum arteriolar sclerotic signs, such as widened arterial reflex, irregularity of lumen

and early crossing signs, were designated as grade  $A_1$ . Advanced vascular disease, with pronounced widening of the reflex stripe and notable nicking, was termed grade  $A_2$ . Evidence of focal vascular insufficiency, such as venous thrombosis or arterial closure, superimposed on changes of the  $A_2$  type, was graded as  $A_3$ . The acute hypertensive signs were evaluated separately. Absence of any acute hypertensive phenomena was diagnosed as  $H_0$ , presence of edema in the nerve fibers, blurring of the disk or pre-organic vessel spasm, as  $H_4$ , hemorrhage or soft exudates, as  $H_2$ , and papilloma with measurable elevation, as  $H_3$ . All patients received both A and H designations, e. g.,  $A_1H_2$  might represent a fundus of early sclerosis with hemorrhage, exudate and vasospasm.

The studies of the fundi tended to confirm the beneficial effects of sympathectomy, since hemorrhages, exudates and papilledema disappeared, but it was significant that acute signs, such as vessel spasm and neural edema, persisted in a large majority of patients despite sympathetic denervation of the vessels of the eye. The degree of arteriolar sclerosis appeared to be of greater prognostic value than other retinal signs in evaluating the decrease in blood pressure to be expected after operation. Patients with the least retinal arteriolar sclerosis showed the best results after sympathectomy. This has emphasized the need for classification that provides adequate evaluation of the arteriosclerotic, as well as the acute, hypertensive phenomena.

<sup>22</sup> Woods, W. W., and Peet, M. M. The Surgical Treatment of Hypertension. II. Comparison of Mortality Following Operation with that of Wagener-Keith Medically Treated Control Cases, *J. A. M. A.* **117**: 1508-1515 (Nov. 1) 1941.



# THE CORNEA

## VII PERMEABILITY TO WEAK ELECTROLYTES

DAVID G COGAN, M.D, AND ERWIN O HIRSCH, B A

BOSTON

Penetration of dissolved material through the cornea is believed to be a function primarily of phase solubility. The epithelium and the endothelium of the cornea are barriers to substances that are not soluble in fats, while the stroma similarly is a barrier to substances not soluble in water. Weak electrolytes require special consideration not only because they include the important group of alkaloids used clinically but because their solubilities in fat and water vary according to their degree of dissociation. In the present paper, studies will be reported on the effect of variations in this dissociation on the penetration of weak electrolytes through the cornea.

Within a range that is characteristic for each substance, weak bases become progressively dissociated with low hydrogen ion concentrations and weak acids with high hydrogen ion concentrations. In the undissociated form (free base) most weak organic electrolytes are fat soluble and variously water soluble, while in the dissociated form (salts) all are water soluble and most are nonfat soluble.

The substances used in studying the effect of dissociation on permeability through the cornea were selected on the basis of freedom from toxic effects, variation in dissociation over an appropriate range of hydrogen ion concentrations and adaptability to quantitative measurement. The weak base aniline and the weak acid salicylic acid were the two electrolytes most thoroughly studied. The degrees of dissociation of aniline and salicylic acid at different hydrogen ion concentrations were determined from the Henderson-Hasselbalch equation, using the dissociation constants of  $4.6 \times 10^{-10}$  and  $1.06 \times 10^{-3}$  respectively.

### THE EXCISED CORNEA

The method employed for measuring permeability of the excised cornea was essentially the same as that previously described<sup>1</sup>. Corneas, with and without epithelium, were attached to the ends of tubes, and the amount of test substance transferred from the tube into the flask was determined at the end of an arbitrary

From the Howe Laboratory of Ophthalmology, Harvard Medical School

1 Cogan, D G, Hirsch, E O and Kinsey, V E. The Cornea. VI Permeability Characteristics of the Excised Cornea, Arch Ophth 31 408 (May) 1944

period of time. The period varied for the different test substances but was always considerably less than that necessary for equilibrium.

The volume of the fluid in the tube was 1 cc in all cases. The concentration of the test substance selected varied with the aqueous solubility of the free base. The fluid in the tube was buffered by the addition to the test solution of two-tenths-molar citric acid or tenth-molar sodium phosphate or suitable mixtures of the two substances. In all cases the fluid in the tube was hypertonic to that in the flask.

The volume of the fluid in the flask was 5 cc and in most of the experiments it was not buffered. So long as the epithelium was present, the hydrogen ion concentration of the fluid in the flask did not vary more than 0.6  $p_H$  unit despite the use of fluids in the tubes with  $p_H$  values ranging from 3 to 10.5. In the absence of the epithelium, however, the  $p_H$  of the flask fluid approximated that of the tube fluid in the course of the experiments.

The hydrogen ion concentration was determined electrometrically for all solutions prior to the experiments and for representative samples of fluid from the tube and from the flask after the experiments.

The major experiments were run in sextuplicate, the average deviation from the mean being  $\pm 10$  per cent.

On the conclusion of each experiment the integrity of the epithelium or the completeness of its removal was checked by transfer of fluorescein.

The amount of aniline transferred was determined photoelectrically by the standard calcium hypochlorite method<sup>2</sup>. Neither the buffer nor the corneal eluate produced any interference. The transfer of salicylic acid was determined photoelectrically, also, by the ferric chloride method. Inasmuch as proteins and salts were found to interfere with the test, the standard colorimetric curve was obtained by adding known amounts of salicylic acid to eluate blanks. Within the range tested both substances obeyed Beer's law, and an accuracy of  $\pm 5$  per cent was attained.

Since the appropriate degrees of dissociation were attained by varying the hydrogen ion concentration of the tube fluid, it was first necessary to establish what range of hydrogen ion concentrations would be tolerated by the epithelium. This was determined by taking advantage of the fact previously observed that the epithelium was an effective barrier to sodium chloride so long as it was intact. A series of tubes holding epithelium-stroma combination were partly filled with a 5 per cent solution of sodium chloride buffered with a phosphate-citrate mixture over a wide range of hydrogen ion concentrations. The transfer of chlorides was measured after eighteen hours. The epithelium

2 Snell, F D, and Snell, C T. Colorimetric Methods of Analysis, New York, D Van Nostrand Company, Inc., 1937, vol 2, pp 408-410

maintained its normal barrier properties during the eighteen hours of the experiment with variations in the  $p_H$  of 3.5 to 10.2. Below and above this range the transfer of chlorides was abnormally increased, and the epithelium was assumed to be damaged.

1, together with the theoretic association curve for aniline. The duration of the experiment was six hours. The greatest amount of aniline transferred was arbitrarily plotted to correspond on

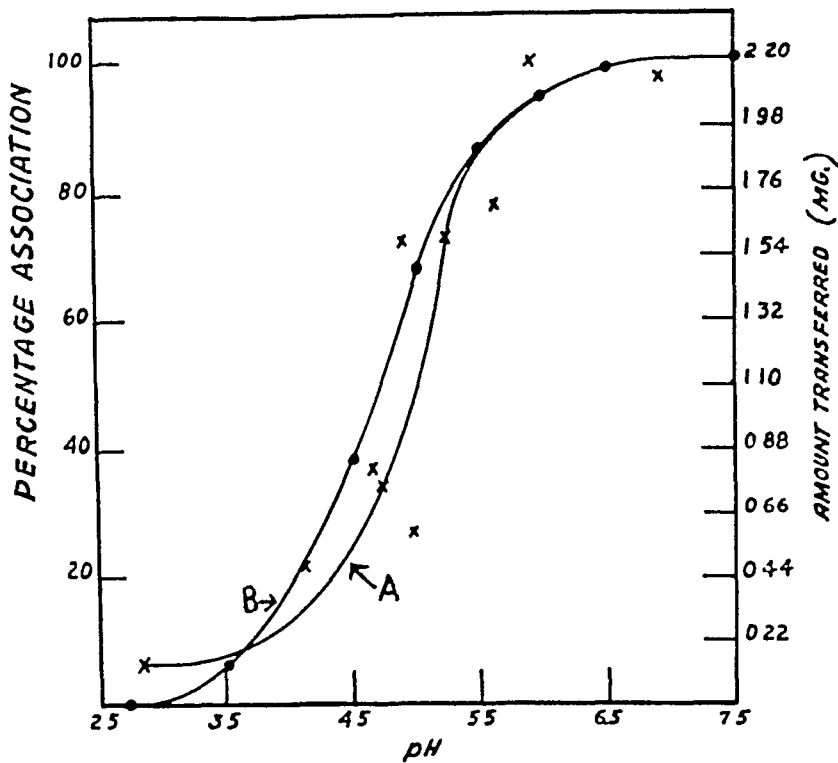


Fig 1—A, average amount of aniline transferred in six hours through the excised cornea from solutions of various hydrogen ion concentrations (phosphate-citrate buffer) B, association of aniline at various hydrogen ion concentrations, determined with the Henderson-Hasselbalch equation

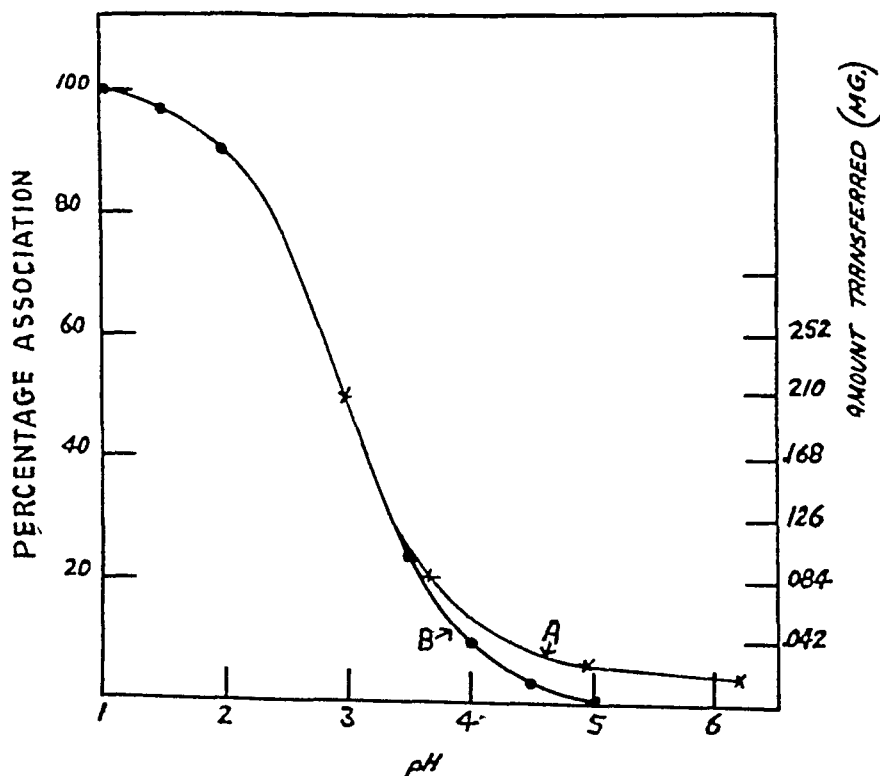


Fig 2—A, average amount of salicylate transferred in two hours through the excised cornea from solutions of various hydrogen ion concentrations (phosphate-citrate buffer) B, association of salicylate at various hydrogen ion concentrations, determined with the Henderson-Hasselbalch equation

The results obtained for the permeability of aniline through the cornea at various values for the  $p_H$  within a range compatible with the integrity of the epithelium are presented in figure

the scale to 100 per cent "association." It will be seen that aniline was transferred across the epithelium-stroma combination according to the amount of undissociated aniline in the test fluid

When stroma only was used, the amount transferred in the test period was approximately the same for all hydrogen ion concentrations

The permeability of the epithelium-stroma combination of the cornea to salicylic acid was similarly plotted in figure 2, together with the theoretic association curve. The duration of the experiment was two hours. Owing to damage to the epithelium, measurements could not be

TABLE 1—Solubility of the Base and Salt of Aniline and of Salicylic Acid in Water and in Fat (Tributyrin)

Test Substance	Solubility, Gm per 100 Cc Solvent	
	Water	Fat (Tributyrin)
Aniline	3.8	Miscible in all proportions
Aniline hydrochloride	107	Less than 0.017
Salicylic acid	0.20	8.2
Sodium salicylate	110	Less than 0.017

made at ranges in the  $p_H$  of less than 3, and here only 50 per cent of the salicylic acid was associ-

appreciably soluble in fats, while the salts, which penetrate poorly, have little fat solubility. Both are soluble in water.

For purposes of comparison, the permeability through excised conjunctiva and sclera was determined for aniline at different hydrogen ion concentrations according to a technic previously described. The results were qualitatively similar to those obtained for the cornea; the conjunctiva acted as a considerable barrier to the transfer of aniline salt but not to aniline base, while the sclera, like the corneal stroma, was relatively freely permeable to both salt and base.

So far as the results with aniline and salicylic acid hold in general for other weak electrolytes, it may be anticipated that weak organic bases penetrate the cornea best at relatively high hydrogen ion concentrations and weak organic acids at relatively low hydrogen ion concentrations. The range over which this variation in the hydrogen ion concentration is effective varies according to the dissociation constant for each

TABLE 2—Penetration Through the Cornea of Several Alkaloids in Solutions Buffered at Different Hydrogen Ion Concentrations

	$p_H$ at Which There is 50% Dissociation	Initial Concentration in Tube, %	Duration of Experiment, Hr	Percentage of Total Test Substance Transferred		Analytic Test
Atropine	9.15	0.2	1½	<0.25 at $p_H$ 4.3	2.75 at $p_H$ 9.0	Pulewka, P. Arch. f. exper. Path. u. Pharmacol. 108: 307-318, 1932
Ephedrine	9.40	5.0	19	4.0 at $p_H$ 5.3	16.7 at $p_H$ 10.1	Chen, K. K. J. Am. Pharm. A. 18: 110-116, 1929
Pilocarpine	7.40	5.0	16	0.4 at $p_H$ 4.5	2.2 at $p_H$ 7.8	The Merck Index, 9th test 1759

ated. The amount transferred at this hydrogen ion concentration, therefore, corresponds on the ordinate of the graph to 50 per cent association. Again it will be seen that there is a close correlation between the association and the permeability curve. In parallel experiments the amount transferred through stroma only was constant for all hydrogen ion concentrations.

To determine whether or not these results are consistent with our previous conclusion that corneal permeability is a function of phase solubility, it is necessary to know the solubilities of dissociated and undissociated aniline and salicylic acid in water and in fat. These were determined by dissolving the free base and the salt in distilled water and in fat (tributyrin) at room temperature. It is assumed that the solvent properties of the fat in the corneal epithelium are not greatly different from those in the more available tributyrin. The results, recorded in table 1, indicate that the free bases of aniline and salicylic acid are similar to other substances which penetrate the epithelium-stroma combination in being

electrolyte, or, more specifically, with the corresponding changes in solubility. From the practical point of view, the most important weak bases are the various alkaloids and the majority of the local anesthetics, while among the more important weak acids are such metabolic products as carbonic acid, lactic acid,  $\beta$ -hydroxybutyric acid and pyruvic acid.

The penetration through the cornea was tested for several common alkaloids, solutions being used which represented two degrees of dissociation, i. e., solutions buffered at different hydrogen ion concentrations. The range of hydrogen ion concentrations over which dissociation occurs is, of course, different for each alkaloid. The hydrogen ion concentration at which 50 per cent dissociation occurs was determined for each alkaloid by electrometric titration, and, as far as possible, permeability tests were made with solutions buffered above and below this value.

Certain difficulties were encountered in measuring corneal permeability to alkaloids which were not previously experienced to any

great extent with aniline. Most important was the instability of the alkaloids, especially in alkaline solutions. It was found, however, that, of the three alkaloids used, atropine showed no significant decomposition for two hours, while ephedrine and pilocarpine were stable for at least twenty hours. These periods were all longer than those used in the experiments.

The results of testing the corneal permeability to atropine, ephedrine and pilocarpine, together with other pertinent data, are presented in table 2. In all cases transfer was greater in the more alkaline mediums, that is, in solutions in which the alkaloid was present to a greater extent in the form of the free base.

The results accord with those Swan and White<sup>3</sup> obtained for penetration of procaine into

the duration of corneal anesthesia with variations in the hydrogen ion concentration of a number of local anesthetics. The results further indicate that the selectivity of corneal permeability, or more especially, of the epithelium, is similar to that which has so abundantly been demonstrated for the individual cell, since Overton<sup>7</sup> first showed that free bases penetrate the cell wall more readily than the salts.

#### THE CORNEA IN SITU

For studies on the intact cornea it was first essential to have a method by which the solution could be kept in contact with the living cornea for any desired time, and since the permeability of the cornea exclusively was being tested, it was essential that the solution should not come in contact with the conjunctiva. The customary

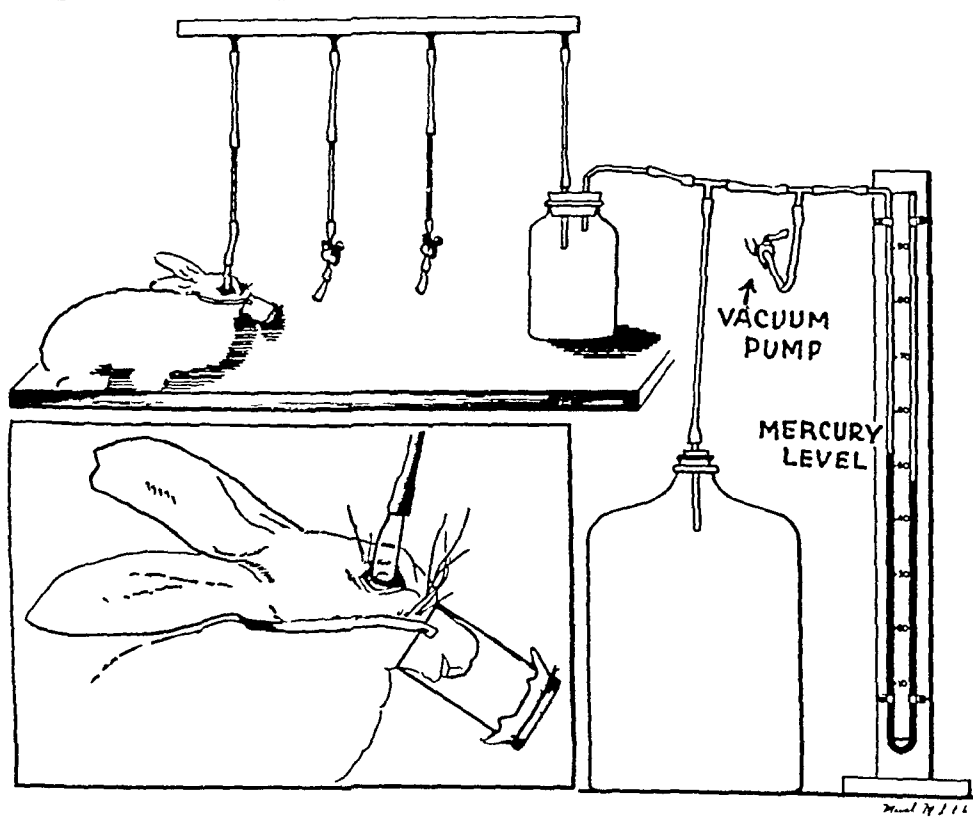


Fig 3—Apparatus employed for holding the eye cup in contact with the cornea in in vivo experiments. The test solution was injected through the rubber tubing at the top of the cup by means of a hypodermic needle after the negative pressure had been applied.

the cornea at different hydrogen ion concentrations and with the observations of Fosdick, Hansen and Dragstedt<sup>4</sup>, Regnier,<sup>5</sup> and Gerlough<sup>6</sup> on

3 Swan, K. C., and White, N. G. Corneal Permeability. I. Factors Affecting Penetration of Drugs into the Cornea, *Am J Ophth* 25 1043, 1942.

4 Fosdick, L. S., Hansen, H. L., and Dragstedt, C. A. The Variation of Anesthetic Efficiency of Procaine Hydrochloride and Procaine Borate with  $p_H$ , *Proc Soc Exper Biol & Med* 27 529, 1923.

5 Regnier, J. De l'augmentation des anesthésies produites sur la corne par alcalinisation des solutions de chlorhydrate de cocaine, *Compt rend Soc de biol* 92 605, 1925.

6 Gerlough, J. D. The Influence of  $p_H$  on the Activity of Certain Local Anesthetics as Measured by the Rabbit's Cornea Method, *J Pharmacol & Exper Therap* 41 306, 1931.

procedure of placing an eye cup on the cornea and sealing its edges with petrolatum failed to secure a water-tight chamber. Pressure of the cup against the cornea was also unsatisfactory not only because of the technical inconveniences but because the procedure caused undesirable vascular congestion.

A method satisfactory for our purposes was obtained by the use of suction. A tube open at one end, with

7 Overton, E. Ueber die osmotischen Eigenschaften der Zelle in ihrer Bedeutung für die Toxikologie und Pharmakologie, *Vierteljahrsschrift der Naturforschenden Gesellschaft in Zürich* 41.383, 1896, Ueber die allgemeinen osmotischen Eigenschaften der Zelle, ihre vermutlichen Ursachen und ihre Bedeutung für die Physiologie, *ibid* 44 88, 1899.

an orifice of 0.8 sq cm (less than the area of a rabbit's cornea), and tapered at the other end was connected with a closed system adjusted to maintain reduced pressure (fig 3). The negative pressure employed was usually 60 mm of mercury, but use of a negative pressure of 300 mm for periods longer than those used in the experiments did not produce any apparent damage to the cornea. The test solution was injected into the tube through the rubber connecting piece at the top of the tube. The amount of test solution was usually 1 cc, but the quantity was not considered critical for the short interval experiments so long as the cornea was adequately covered. The hydrogen ion concentration of the test solution was controlled by the phosphate-citrate buffer.

The solution was kept in contact with the cornea for four minutes. At the conclusion of this time, the tube was removed, and the surface of the eye was thoroughly irrigated with a 1 per cent solution of

aniline through the living rabbit's cornea shows the same variation with dissociation as was previously found for the excised cornea.

#### DISSOCIATION CONSTANTS, SOLUBILITIES AND PERMEABILITIES OF VARIOUS ALKALOIDS

Direct experimental investigation of any large number of alkaloids in a manner similar to that already described for aniline is impracticable in view of the lack of reliable quantitative tests for, and the instability of, most of the alkaloids. Nevertheless, sufficiently accurate tests have been made with atropine, ephedrine and pilocarpine to make it reasonably certain that the results with aniline and salicylic acid are generally applicable provided there are taken into account the dissociation constants and the corresponding changes in solubility in fats and in water. To our knowledge, the dissociation constants of the alkaloids under consideration are only partially available, and data regarding their solubilities in fats (not to be confused with the ordinary organic solvents) are nowhere available. For purposes of reference, therefore, we have undertaken to determine the dissociation constants of some of the alkaloids commonly used and to measure the solubility of each base and of at least one of its salts in water and in tributyrin.

The dissociation constants of the alkaloids were obtained by back titration of the salt with sodium hydroxide. Either the salts were previously purified by repeated recrystallization from cold alcohol until a constant melting point was obtained, or the alkaloid was purified by recrystallization until a constant melting point was obtained and the base was then dissolved in an equinormal solution of an acid and titrated. The  $p_H$  at which 50 per cent dissociation occurs was determined by half-neutralization. While this is strictly tenable for the monobasic alkaloids only, it is approximately correct for the polybasic alkaloids (physostigmine and pilocarpine) also, the dissociation constant of the second basic group is negligible for our purposes. The point at which 50 per cent dissociation occurs is familiarly designated by the equation  $p_H = 14 - pK_B$  and affords a convenient point of reference for estimation of permeability with variations in the hydrogen ion concentration.

The solubilities of the alkaloids and their salts in water and in tributyrin are given in table 3.

The values for the solubility in water were obtained largely from the Pharmacopeia of the United States<sup>8</sup> and the Merck Index<sup>9</sup>. In the

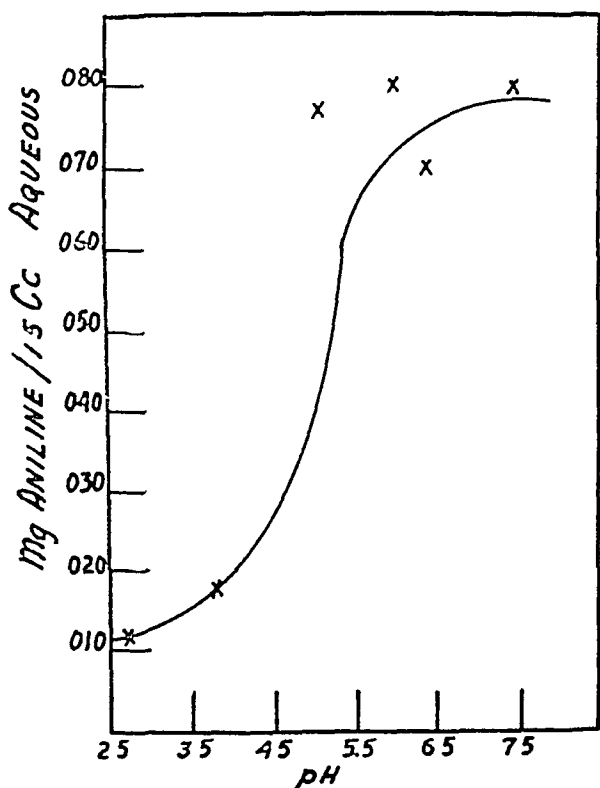


Fig 4 — Concentration of aniline in the anterior chamber after four minutes when 1 per cent aniline in a 1.5 per cent solution of sodium chloride was placed outside the cornea.

sodium chloride and the cornea examined for possible damage by means of the fluorescein stain. Then 0.15 cc of aqueous was withdrawn in a microsyringe and analyzed for the test substance.

It was first established by means of fluorescein staining that the living rabbit's cornea would tolerate a 2 per cent solution of sodium chloride the  $p_H$  of which was controlled within the range of 3 to 12 for contact periods of at least five minutes by buffering with a two-tenths-molar phosphate-citrate solution.

One per cent of aniline in a 1.5 per cent solution of sodium chloride was used as a test solution.

The results are presented graphically in figure 4, each point representing the average of two experiments. It is obvious that the transfer of

<sup>8</sup> Pharmacopeia of the United States of America, twelfth revision, Easton, Pa., Mack Printing Company, 1942, pp 604-605.

<sup>9</sup> The Merck Index, ed 5, Rahway, N J Merck & Company, Inc, 1940.

case of epinephrine, for which no data were obtainable, the aqueous solubility was determined separately

The solubilities of the alkaloids in tributyrin were measured as follows

Sufficient concentrations of the alkaloid were obtained in hot tributyrin so that a precipitation occurred when the solution was cooled to room temperature. Two cubic centimeters of the supernatant tributyrin was then extracted repeatedly with a normal solution of hydrochloric acid until the extractant gave no precipitation with excess ammonium hydroxide. The further procedures were those commonly employed for the purification and determination of alkaloids<sup>8</sup>. The only variation from this procedure occurred in the case of epinephrine, for the identification of which, owing to its low solubility in tributyrin, the more sensitive Viale test was used.

The solubilities of the alkaloid salts in tributyrin were measured similarly except that the aqueous extractant was treated with red mercuric iodide (Valser's reagent) instead of the less sensitive ammonium hydroxide. The extraction was considered complete when the extractant no longer gave a precipitate. Again, the only exception occurred in the case of epinephrine.

The data obtained, presented in table 3, should provide the information necessary to determine what alkaloids approach the optimum conditions for permeability through the cornea.

TABLE 3—*Solubilities of the Alkaloids in Water and in Tributyrin*

Test Substances	$p_H$ at Which 50% is Dissociated (14 — $p_{Kb}$ )	Solubility, Parts per 100 Gm. of Solvent *	
		Water	Fat (Tributyrin)
Epinephrine		0.0101	0.00003
Epinephrine hydrochloride	8.50	100.0	0.00003
Atropine		0.15	0.28
Atropine sulfate	9.00	250.0	0.007
Cocaine		0.17	9.5
Cocaine hydrochloride	8.62	252.0	0.002
Ephedrine		5.0	33.0
Ephedrine sulfate	9.15	33.0	<0.005
Eucatropine		1.3	0.47
Eucatropine hydrochloride	9.58	>100.0	0.007
Homatropine		1.001	0.36
Homatropine hydrobromide	9.60	16.6	0.004
Physostigmine		1.001	6.0
Physostigmine salicylate	7.7	1.3	0.008
Pilocarpine		100.010	Miscible
Pilocarpine nitrate	7.11	25.0	<0.001
Procaine		1.001	23.0
Procaine hydrochloride	8.90	166.0	<0.005

\* The solvent was kept at room temperature (23°C)

#### COMMENT

The foregoing data on aniline, salicylic acid and alkaloids indicate that the organic bases penetrate the cornea while their salts do not. This corroborates the previous observation that the corneal epithelium and endothelium are bar-

riers to substances not soluble in fats. There are, however, other considerations which vitiate the immediate application of these results to the local use of drugs. Especially noteworthy is the instability of the aqueous alkaloid solutions unless acidified. Moreover, the tears, having considerable buffer capacity, will determine the hydrogen ion concentration of the weak solution as soon as it is instilled in the eye, so that the  $p_H$  of the original solution is not important. Nothing is gained, therefore, by applying solutions of the base, rather than of the salts, to the eye, and much may be lost by decomposition of the drug.

From the practical consideration of permeability through the cornea, some weak electrolytes used in therapy may be considered more suitable than others, it may be possible to synthesize drugs having the optimal prerequisites. The most important considerations for permeability are the dissociation constant and its bearing on fat solubility. The dissociation constant of the "ideal" alkaloid would be sufficiently low so that the alkaloid would be present in the completely undissociated state at physiologic hydrogen ion concentrations. Thus, one would expect pilocarpine and physostigmine to be absorbed through the cornea at  $p_H$  7 more effectively than are atropine, homatropine and ephedrine. A notable exception is epinephrine, which, even in the undissociated state, is practically insoluble in fats<sup>10</sup>. Similarly, the dissociation constant of the "ideal" weak acid would be sufficiently low so that it, also, would be present in the undissociated state at physiologic hydrogen ion concentrations. Obviously, salicylic acid, which was the weak acid most studied, is far from fulfilling this prerequisite.

To the extent that the drug is not present on the cornea in the undissociated state it will, of course, not be efficiently absorbed in the eye, and in passing through the nasolacrimal and the gastrointestinal tract it may be absorbed in sufficient quantity to produce undesirable systemic reactions, such as are common with atropine drops. These factors, which are concerned in the choice of drugs that will penetrate the cornea, do

<sup>10</sup> An experiment was undertaken to compare the permeability of epinephrine base and that of a salt of the drug through the excised cornea, but the results were not included in the tables of the text, as they were not quantitative. Little base could be dissolved in the tube fluid, and the Viale test made on the flask fluid after twenty hours merely indicated the absence or the presence of epinephrine in small amounts. Qualitatively, it was apparent that an extremely small amount of epinephrine, even in the form of the base, penetrated through the cornea as long as the epithelium was present.

not appear to have been previously considered in ophthalmic therapeutics

#### SUMMARY

1 Permeability through the excised cornea of various weak organic electrolytes (aniline, salicylic acid, atropine, pilocarpine and ephedrine) is a function of the degree of dissociation of the electrolyte. The free base penetrates the epithelium-stroma combination, while the salt penetrates the stroma only. Similar results were obtained with a conjunctiva-sclera combination. This effect of dissociation on permeability is attributed to the difference in solubility in fats

and is held to support the previous thesis that substances penetrate the epithelium only so far as they are soluble in fat

2 Permeability of aniline through the intact cornea in vivo is, similarly, a function of dissociation

3 A knowledge of the dissociation constant and solubility properties of an alkaloid enables one to predetermine its permeability through the cornea

Dr Margaret Holt assisted in measuring the physicochemical constants of the alkaloids and in some of the experiments on permeability

243 Charles Street

# CARBAMINOYLCHOLINE CHLORIDE IN THE TREATMENT OF GLAUCOMA

DANIEL KRAVITZ, M D

BROOKLYN

Until the causes are found, glaucoma, acute and chronic, will be a never ending source of worry to the ophthalmologist, as well as to the patient. The results, even with the best of therapy, all too often are disastrous. Ophthalmologists are therefore on a continuous lookout for new therapeutic methods, both medical and surgical.

In the last few years the greatest advance in the medical treatment of glaucoma has been the synthesis of a large group of cholinergic drugs: mechylol, neostigmine, furfuryltrimethylammonium iodide and, the latest, carbaminoylecholine chloride.

Carbaminoylecholine chloride is a synthetic choline derivative which acts principally by inducing parasympathetic stimulation. Its chemical structure is similar to acetylcholine, and, according to O'Brien and Swan,<sup>1</sup> its action is more prolonged because its hydrolysis is slow and it is therefore more stable in the tissues. Used experimentally on isolated sphincter of the iris, it is one of the most powerful of miotics.

Velhagen<sup>2</sup> found that carbaminoylecholine chloride contracted the sphincter of the pupil in high dilutions, that it reduced intraocular tension and blood pressure and that these effects were antagonized by atropine. According to him,<sup>3</sup> a 0.75 per cent solution of carbaminoylecholine chloride produces greater miosis than a 2 per cent solution of pilocarpine but slightly less miosis than a 0.25 per cent solution of physostigmine. However, he found that a 0.75 per cent solution of carbaminoylecholine chloride had less effect on accommodation than a 2 per cent solution of pilocarpine.

Carbaminoylecholine chloride is also a powerful dilator of the peripheral vascular system.

1 O'Brien, C. S., and Swan, K. C. Doryl in the Treatment of Glaucoma Simplex, *Tr. Am. Ophth. Soc.* **39** 175-193, 1941.

2 Velhagen, K. Die Grundlagen der okularen Pharmakologie und Toxikologie des Carbaminoylecholins (Lentin, Doryl), *Arch. f. Augenh.* **107** 319, 1933.

3 Velhagen, K. Die praktische Verwendbarkeit des Doryls (Carbaminoylecholin) in der Glaukombehandlung, *Klin. Monatsbl. f. Augenh.* **92** 472 (April) 1934.

Swan and Hart<sup>4</sup> observed an elevation of temperature in the anterior segment of the eye, indicating an increased blood supply to the part. They found this effect to be greater with this substance than with any of the other cholinergic drugs. Theoretically this action should contraindicate its use in treatment of acute and subacute glaucoma, but clinical experience has not entirely borne out this conclusion.

De Sanctis<sup>5</sup> reported on the effects of carbaminoylecholine chloride on different types of glaucoma. He obtained good results only in cases of chronic glaucoma. The drug had no effect in cases of acute glaucoma even if used in 15 per cent solution, but he obtained favorable results in the same cases with neostigmine and mechylol. The reason for the failure may have been faulty application of the drug.

Recently Swan and White<sup>6</sup> have shown that the absorption of carbaminoylecholine chloride through the cornea is inconstant and undependable. If, however, the drug is prescribed in a wetting agent, such as zephiran, its absorptive quality is greatly increased. If, in addition, the eye is massaged through the lids for a few minutes after instillation of the drop, the absorption is further increased.

When used as drops carbaminoylecholine chloride has little effect on the system. However, parenteral administration of too large doses has recently caused a number of deaths. In large doses it causes flushing of the face, vascular dilatation, decrease in blood pressure, increase in pulse rate, basal metabolic rate and respiratory volume, sweating, salivation, and increased peristalsis.

At present, carbaminoylecholine chloride has found its greatest use in treatment of chronic glaucoma, especially in cases in which the dis-

4 Swan, K. C., and Hart, W. M. Comparative Study of Effects of Mechylol, Doryl, Eserine, Pilocarpine, Atropine and Epinephrine on Blood-Aqueous Barrier, *Am. J. Ophth.* **23** 1311 (Dec) 1940.

5 de Sanctis, G. E. L'azione del doryl sull'occhio in condizioni normali e in casi di glaucoma, *Ann. di ottal. e clin. ocul.* **65** 25 (Jan) 1937.

6 Swan, K. C., and White, N. G. Corneal Permeability Factors Affecting the Penetration of Drugs into the Cornea, *Am. J. Ophth.* **25** 1043 (Sept) 1943.



ease does not respond to pilocarpine or to physostigmine. It is also valuable as an agent to induce rest when the condition has ceased to respond satisfactorily to these drugs. After a few months' treatment with carbaminoylecholine chloride the eye usually reacts well again to the weaker miotics. The drug has also been used to good effect in aborting an attack of acute glaucoma.<sup>7</sup> It may also be used when other miotics have produced sensitivity of the conjunctiva or dermatitis of the skin of the lids.

The dose varies with each case and must be decided individually. As a rule, a 0.75 per cent solution has slightly more effect than a 2 per cent solution of pilocarpine nitrate and about the same effect as a 0.25 per cent solution of physostigmine salicylate. At first it should be given as often as the other drugs were to be prescribed, and then the frequency of instillation should be reduced. Usually it will be found that the drug can be instilled less often than, and with the same effects as, pilocarpine or physostigmine. This is because it is so slowly hydrolyzed in the tissues and therefore acts for a longer time. Swan<sup>8</sup> showed that when it is prescribed in petrolatum its effects can be still further prolonged, and so it may be instilled less often, with the same results. With carbaminoylecholine chloride, the patient usually complains of greater blurring of vision, and for a longer period than with the other miotics. In some cases this troublesome effect disappeared spontaneously after prolonged use.

#### REPORT OF CASES

**CASE 1**—D S, a man aged 23, came to the office on Feb 15, 1942, because of sudden loss of vision in the right eye two weeks before. He had had poor vision since birth. About six or seven years before he consulted me, a cataract had suddenly developed in the left eye. An operation was performed, but vision never returned. Two weeks prior to his consulting me there was sudden loss of sight in the right eye, in which until that time vision had been sufficient to enable him to work. He was now practically blind.

With the right eye large objects were seen as shadows. There was complete aniridia. The lens was swollen and diffusely milky. The eye was buphthalmic, although tension was 20 mm (Schiotz). Vision in the left eye was limited to uncertain light perception. There was complete aniridia. A staphyloma involved the ciliary body above. The fundus was not visible. Tension was 3 plus.

The patient was admitted to the Brooklyn Eye and Ear Hospital on March 11 for linear extraction of the lens of the right eye. The postoperative course was uneventful, and he was discharged from the hos-

pital on March 21. On March 29 vision was 20/200 with a correction of +8.00 D sph  $\subset$  +3.00 D cyl, axis 150. On April 2 the patient came to the office stating that he had severe pain in the right eye all night. He said that the same thing had happened to the left eye after operation. Tension was 4 plus, and vision was reduced to perception of shadows. A mixture of 1 per cent physostigmine salicylate and 2 per cent pilocarpine nitrate was prescribed for instillation, but tension could be reduced only to 2 plus. Neostigmine bromide had no better effect. On April 7 the pain had become more severe, and tension was further increased. Carbaminoylecholine chloride, 0.25 per cent, was prescribed, to be instilled every four hours, and the next day tension was reduced to 20 mm. The patient has since been using this substance in the morning and at night only, and the condition has been kept under control. The patient has been able to work at his usual trade.

**CASE 2**—H S, a woman aged 55, came to the outpatient department of the Brooklyn Eye and Ear Hospital, in the service of Dr Walter V. Moore, on Feb 25, 1941, because of gradual loss of vision in the right eye.

Examination showed a mature cataract in the right eye, with reduction of vision to shadows. Posterior cortical changes were present in the lens of the left eye. Vision was 20/40 with correction. A complete medical examination revealed nothing pathologic, and no foci of infection were encountered. As vision in the left eye deteriorated rapidly, she was admitted to the hospital for extraction of the right lens.

A combined intracapsular extraction was performed on July 3, 1941. There were no complications at the time of operation, and the postoperative course was uneventful. She was discharged on July 13, with corrected vision of 20/40. On July 26, 1941 tension in the right eye was 50 mm (Schiotz), and in spite of the use of physostigmine and pilocarpine, it rose to 65 mm.

On Sept 7, 1941 cyclodialysis was performed, and the tension dropped to 22 mm for a few weeks, but on October 11 it was 35 mm and rose, in spite of the use of miotics, to 65 mm. A second cyclodialysis was therefore performed, on Feb 2, 1943. The tension dropped to 26 mm and stayed at that level for several weeks, after which it again rose to 45 mm.

In the early part of March 1943, a prescription for 1 per cent carbaminoylecholine chloride was given the patient, but she continued to use pilocarpine and physostigmine. Finally on Feb 1, 1944, she decided to have the prescription for carbaminoylecholine chloride filled. The tension promptly dropped to 13 mm, and it has stayed at that level since. At first the drops were instilled every four hours, but at present they are being used three times a day.

**CASE 3**—S G, a man aged 46, came to the office on Oct 10, 1935, because of difficulty in reading. He had been wearing glasses for over forty years. Vision in the right eye was 20/70 and was improved to 20/20 with correction. He had convergent strabismus in the left eye, a condition which had been present since childhood. Vision in that eye was 20/100 and was improved to 20/70 with correction. Bifocal glasses were prescribed and were checked in November 1939 and December 1940.

He came to the office again on July 13, 1943, because of blurring of the right eye. He stated that for the past several months he had been colliding with people coming from his right. There was no history of seeing halos around lights, but he had occasional episodes of

<sup>7</sup> Clarke, S. T. The Use of Doryl in the Treatment of Glaucoma, *Am J Ophth* 25:309 (March) 1942.

<sup>8</sup> Swan, K. C. Carbaminoylecholine Chloride in Petrolatum, *Arch Ophth* 30:591 (Nov) 1943.

blurred vision and slight headaches in the right temporal area

Vision in the right eye was still 20/20 with the glasses previously prescribed. The cornea was moderately steamy, but the pupil was not more dilated than that of the other eye. There were deep cupping of the optic disk and notable contraction of the visual field. Tension was 55 mm in the right eye and 20 mm (Schiotz) in the left eye, with no evidences of glaucoma in the left eye.

A 1 per cent solution of physostigmine salicylate with 2 per cent pilocarpine nitrate was prescribed, and the next day the tension was reduced to 35 mm. Further reduction, however, could not be effected. On July 18 an Elliot trephine operation was done at the Brooklyn Eye and Ear Hospital, and the tension dropped to 18 mm (Schiotz). The tension remained at that level until October 10, when it rose to 35 mm and the field became slightly more contracted. Physostigmine or pilocarpine or the two combined, and later neostigmine, failed to reduce the tension. In fact, it rose three days later to 40 mm, in spite of the presence of a bleb and apparent good drainage.

On December 4 a 0.75 per cent solution of carbaminoylcholine chloride was prescribed, to be instilled every four hours. The tension slowly fell, until by December 16 it was 26 mm. The tension remained at that level until January 21, when it suddenly dropped to 20 mm. It has fluctuated between 25 and 20 mm since, and the field has enlarged so that it is not more contracted than before the operation.

The patient complained of blurred vision, which lasted almost two hours each time the drops were instilled. Since the early part of March the time of troublesome blurring has been reduced to less than half an hour.

CASE 4—S. L., a man aged 41, had been under the care of another ophthalmologist for eight years because of chronic glaucoma of both eyes. On June 1, 1943 an Elliot trephine operation was performed on both eyes. The postoperative tension in both eyes remained high, even though the patient had been using a mixture of physostigmine and pilocarpine every three hours since the operation. Because the patient found it too difficult to travel, he came under my care, on Nov. 12, 1943.

Vision was 20/40 in the right eye and 20/30 in the left eye. There was no notable cupping of either disk, and the fields were normal. The tension was 35 mm (Schiotz). In order to study the eyes, I asked him not to use the drops for one day. The next day the tension rose to 55 mm in the right eye and to 45 mm in the left eye. Administration of the drops was again instituted. The tension fluctuated between 30 and 35 mm, although the instillations were made every three hours.

On November 26, a 0.75 per cent solution of carbaminoylcholine chloride, to be used every three hours, was prescribed. The tension fell rapidly. At present the patient is using an ointment containing 1 per cent carbaminoylcholine chloride at night and 3 drops of the solution in the right eye and 2 drops in the left eye daily. The tension has remained consistently at 25 mm (Schiotz). Vision and the visual fields have remained unchanged.

In spite of the frequency of its use, carbaminoylcholine chloride has caused no troublesome blurring. In fact, the patient states that there is a feeling of well-being in the eyes after its use.

CASE 5—M. T., a man aged 57, came to the office on Dec. 11, 1943, complaining of severe pain in the left eye for about a week. About two years before the patient had an attack of acute glaucoma in that eye, and an iridencleisis was performed by another ophthalmologist. Evidently the tension in that eye had not been reduced by the operation because he had been using a 2 per cent solution of pilocarpine nitrate three times a day. Vision in the left eye had not been good, and about two weeks before his visit to the office the eye became red and painful, and vision was reduced.

Examination of the right eye revealed vision of 20/20 and a tension of 20 mm (Schiotz). The left eye was extremely red and the cornea steamy. A knuckle of iris was present under the conjunctiva at 12 o'clock. A hypopyon was present in the lower fourth of the anterior chamber. The fundus reflex was not obtainable, and the eye was soft.

A diagnosis of panophthalmitis was made, and the probability of enucleation was discussed. The patient was admitted to the Brooklyn Eye and Ear Hospital the next day, and large doses of sulfadiazine were prescribed. Several intravenous injections of typhoid-paratyphoid vaccine were also given. On the fourth day a tension of 50 mm (Schiotz) developed in the right eye. This was controlled by several instillations of mecholyl chloride and neostigmine bromide. A tension of 20 mm was subsequently maintained with instillations of a 2 per cent solution of pilocarpine nitrate every four hours. The patient was discharged from the hospital on December 19. The left eye was white, and the hypopyon had entirely disappeared. A large exudate could be seen in the vitreous.

Several days later the patient went to Dr. Mark J. Schoenberg for consultation. While he was at the physician's office, an acute attack of glaucoma developed in the right eye. A bead of ointment containing 1 per cent carbaminoylcholine chloride in anhydrous white petrolatum was placed in the eye, with rapid subsidence of the attack. When the patient was seen the next day at the office, tension in the right eye was 18 mm, although the eye had received no other medication since instillation of the carbaminoylcholine chloride ointment. In this case the drug aborted an attack of acute glaucoma more rapidly, and for a longer period, than any other medicament. A normal tension has since been maintained with instillations of a 2 per cent solution of pilocarpine nitrate every four hours.

The left eye is entirely white, the tension is normal, vision is 20/50—, and there is a fine membrane in the pupillary area. The result is unusually gratifying in a case of late infection after iridencleisis and compares well with other good results in cases of infection following operation.<sup>9</sup>

An unexplained action of carbaminoylcholine chloride has been its relief of pain without reduction of tension in some cases.

CASE 6—A. S., a woman aged 65, came to the office on March 24, 1944, with a history of sudden onset of pain and loss of vision in the right eye and vomiting. She went to an ophthalmologist, who gave her drops, but the pain was not relieved, and the next day he advised immediate operation.

9 Kravitz, D., and Duest, L. J. Postoperative Endogenous Infections of the Eye with Recovery, *Am J Ophth* 27:167 (Feb.) 1944, correction, *ibid* 27:303 (March) 1944.

Examination revealed that the right eye was red. The cornea was steamy and the pupil only moderately dilated. The fundus was not visualized. The tension was 95 mm (Schiotz). The left eye had vision of 20/30 and a tension of 20 mm. Operation was advised, and until the patient made up her mind, an ointment containing 1 per cent carbaminoylecholine chloride, to be instilled into the eye at night before retiring, was prescribed. In addition, she was to use a mixture of pilocarpine and physostigmine, given by the other ophthalmologist, every four hours.

The next day the patient was entirely relieved of pain, though the tension and appearance of the eye were unchanged. She has remained free of pain and now maintains that because there is no pain operation is unnecessary, and she cannot be persuaded to enter the hospital.

CASE 7 (reported by permission of Dr. D. A. Ajello)—M. A., a man aged 67, was first seen on Nov. 4, 1942, with a history of having been treated for glaucoma in both eyes for over three years. He came because of severe pain over the right temporal area and much more severe pain over the left eye.

Examination showed that the patient was completely blind in both eyes. The right eye had a tension of 4 plus. The left eye presented panophthalmitis, with imminent rupture of the cornea. The left eye was removed the next day, and use of miotics in the right eye was continued. The patient continued to complain of severe pain. A few days later there developed a rash on both lids and conjunctival edema. The condition persisted, whether pilocarpine or physostigmine was used. On consultation with me, carbaminoylecholine chloride was prescribed.

The patient was given a 0.75 per cent solution of the drug, to be used three times daily. Within two days the tension was lowered to 2 plus, but he complained of severe pain over the eye for about an hour after each instillation. He was advised to use the drops on arising and just before retiring. Since then he has been entirely free of pain and headaches and of symptoms after instillation of the drops, although the tension remains at 2 plus.

CASE 8—R. B., a woman aged 59, came to the office on Aug. 15, 1938. She had had an acute attack of glaucoma in the left eye the evening before. Her son, who is a physician, recognized the symptoms and immediately and repeatedly instilled a 0.5 per cent solution of physostigmine salicylate, so that when I saw her, the tension was 16 mm in that eye and 20 mm in the right eye (Schiotz). The pupil was moderately and irregularly dilated, and the eye was somewhat tender to touch but was of normal appearance. The visual fields were normal. Vision was 20/30 in the right eye and 20/25 in the left eye with correction.

The patient was seen at regular intervals. The pressure in the left eye fluctuated between 35 and 22 mm (Schiotz), but the fields and vision remained good. However, the disk began to appear cupped as time went on.

On Feb. 1, 1940, an Elliot trephine operation was performed on the left eye at the Beth Moses Hospital, after which the pressure dropped to 20 mm. The pressure in the eye has remained at that level, and the fields and visual acuity have not changed.

On Sept. 14, 1939 the tension in the right eye rose to 30 mm (Schiotz). This was easily controlled with a 2 per cent solution of pilocarpine nitrate, instilled four times a day. Inasmuch as vision remained good and the fields were unchanged, conservative treatment was followed.

During January 1941 the right disk began to appear cupped, and operation was advised. This the patient refused because her son had just joined the armed forces, and so she was kept under close observation. The tension in that eye fluctuated between 30 and 22 mm, but vision remained unchanged, and the fields were only slightly constricted.

On Sept. 2, 1943 a severe attack of acute glaucoma developed. The eye was stony hard and could not be reduced by miotics of any kind. The next day a basal iridectomy was done at the Brooklyn Eye and Ear Hospital, with a good immediate result.

On October 11 the lens began to swell and the tension to rise. These symptoms became rapidly worse, so that an extracapsular extraction was necessary. This was done at the Brooklyn Eye and Ear Hospital on Nov. 12, 1943. Remnants of capsule remained in the anterior chamber and could not be removed. Healing was uneventful. The tension remained normal until Jan. 31, 1944, on which day she complained of a pain in the eye and a feeling as if there were a lump on the eye. The tension was 60 mm (Schiotz).

A 1 per cent solution of carbaminoylecholine chloride, to be used every four hours, was prescribed. The next day the sensation of a lump and the pain had entirely subsided, but the tension was unaffected. Since then the tension has varied from 40 to 70 mm, but at no time has the patient had any discomfort in that eye.

## CONCLUSION

Carbaminoylecholine chloride is not a panacea for all the ills of glaucoma. The cases here presented are fairly representative of almost all the forms of glaucoma that may be encountered. The drug has been effective in relief of all types. In some cases, however, it has not produced good results. In a case of glaucoma following an intracapsular extraction, in the service of Dr. Walter V. Moore, the intraocular tension rose during treatment with carbaminoylecholine chloride. However, no other medication had been effective, and subsequently a cyclodialysis was performed.

Carbaminoylecholine chloride is a valuable addition to the armamentarium for the treatment of glaucoma, and it may give brilliant results when other drugs have failed. Because of the troublesome and prolonged blurring, and sometimes pain, following its use, pilocarpine, physostigmine, mecholyl and neostigmine should first be tried.

861 Park Place

# LIPOCHONDRODYSTROPHY

(DYSOSTOSIS MULTIPLEX, HURLER'S DISEASE), PATHOLOGIC CHANGES  
IN THE CORNEA IN THREE CASES

LIEUTENANT MICHAEL J HOGAN (MC), U S N R,  
AND FREDERICK C CORDES, M D

SAN FRANCISCO

Lipochoondrodystrophy is a rare disease of congenital origin and uncertain cause. It is characterized by chondrodystrophic changes in the skeleton and deposition of a lipid-like substance in many of the body tissues, including the cornea.

The first signs of the disease usually appear toward the end of the first year of life, when dorsolumbar kyphosis and enlargement of the head make their appearance. As the condition progresses numerous developmental failures appear. The child learns to walk, talk and feed itself at a later age than normal. By the age of 4 years normal growth has usually ceased, and the complete picture of the disease has become apparent. The head is enlarged, the face shows wide-set, protuberant eyes and a saddle nose and there is thickening of the lips and tongue. The neck is very short and the chest poorly developed. There are a protuberant abdomen, with an umbilical hernia, and enlargement of the liver and spleen. The joints of the hands, wrists, elbows and hips present deformities and limitation of motion. The hands are broad and thick. These bodily changes give the child a gargoyle-like appearance.

Roentgenographic studies show characteristic changes. The skull is usually enlarged and scaphocephalic. In a large number of cases the sella turcica is greatly elongated, due to maldevelopment of the sphenoid bone. Irregularities, fragmentation and enlargement of the ends of the shafts of the long bones are almost always noted. There is dorsolumbar kyphosis, with narrowing and flattening of the vertebral bodies in this portion of the spine. A distinctive clouding or haziness of the corneas occurs in over 75 per cent of cases. When it is present, it is considered diagnostic of the disease. In most cases this cloudiness appears before the age of 3 years. Instances have been reported in which it was present at birth. On inspection with focal illumination the

corneas have a ground glass appearance and are diffusely hazy. There is no tendency for the eye to be inflamed or for the cornea to become vascularized. With the slit lamp the haze is resolved into uniformly distributed tiny, gray or yellow-gray dots, which at first occupy the middle and deeper layers of the cornea. Later they are distributed throughout the stroma. These dots do not appear to be crystalline and are only slightly refractile. After a certain stage of opacification is reached, the cornea remains unaltered. Vision is reduced correspondingly as the opacification proceeds. Hyaline or calcareous degeneration of this material in the cornea has not been reported. The intraocular tension is usually normal. Studies of the blood fats usually reveal no abnormality.

## PATHOLOGIC CHANGES

There are three published reports in the literature of pathologic studies of the eyes in cases of lipochoondrodystrophy.

The first report was made by Kressler and Aegerter,<sup>1</sup> in 1938. In their case all the signs of lipochoondrodystrophy were presented. Clouding of the corneas was first noted by the parents when the child was 4½ months of age. The authors first examined the patient at the age of 6½ years, at which time the corneas were opaque. The child died of heart disease at the age of 7½ years. At autopsy all the organs except the kidneys showed extensive fatty infiltration. Many of the ganglion cells of the cerebral cortex, the basal ganglia and the brain stem were balloon shaped, with puffing of the axons and dendrites. The cytoplasm had a netlike structure, in which there were fine, dark blue granules which did not take stains for fat. The glia cells of the cortex contained lipid, as did those in the white substance. Many attempts were made to stain the material which produced vacuoles in the cells of all the other tissues. The results, however, were not conclusive.

Histologic examination of the eyes showed that the lamellae of the cornea proper were widely separated and that there was no cellular infiltration. The authors were uncertain as to whether this separation was an artefact secondary to fixation or the result of edema or infiltration. All the other ocular structures appeared normal. The report did not state whether any attempt was made to stain the corneal tissues for fat.

1 Kressler, R J, and Aegerter, E. Hurler's Syndrome (Gargoylism), *J Pediat* 12 579, 1938.

From the Division of Ophthalmology, University of California Medical School.

This study was made possible by a fund from the Mrs E S Heller Donations.

The second report was made by Berliner,<sup>2</sup> in 1939. His patient died at the age of 5 years, after repair of an umbilical hernia. A photograph of the patient demonstrates all the typical features of lipochondrodystrophy. Examination showed extensive opacification of all the corneal layers, without vascularization. Vision was approximately 10/200 in each eye. The intraocular tension measured 14 mm of mercury (Schiotz) in each eye, and the corneas appeared larger than normal. Pyroxylin sections of the eye were prepared and stained by various technics. Stains of gelatin mounts of corneal sections for neutral fat gave negative results. The deeper and central areas of the cornea, corresponding to the main opacification seen clinically, gave a paler reaction to all the stains. Bowman's membrane was missing in places and was replaced by cells containing a vacuolated cytoplasm, the cells varying from spindle shape to globular. The corneal nuclei lay in spindle-shaped, vacuolated spaces. In the deeper, central regions of the cornea these vacuolated spaces contained granular material. Berliner expressed the opinion that this material was composed of lipid granules and that the presence of these granules refuted any claim that the spaces were the result of artefacts. The granules were well brought out with Masson's stain and with hematoxylin and eosin and were similar in appearance to those observed in other organs. The rest of the eye showed no abnormality.

The third pathologic report was made by Rochat,<sup>3</sup> in 1942. In his case, which had been reported previously (1940) from the clinical standpoint by Waardenburg,<sup>4</sup> pronounced diffuse clouding of the corneas, together with all the other changes characteristic of lipochondrodystrophy, was present. Waardenburg removed one eye at autopsy and sent it to Rochat for pathologic examination. The eye was fixed in a dilute solution of formaldehyde. One portion was used for frozen sections, and the other was embedded in paraffin. The only changes encountered in the eye were those in the cornea. The corneal epithelium and stroma and Descemet's membrane were normal. In Bowman's membrane, however, numerous defects were scattered across the whole cornea. In these defects were large cells containing abundant protoplasm and well stained nuclei. The protoplasm contained numerous glistening granules. At times these granules were confluent, producing the appearance of snowflakes. The granules were soluble in ether and alcohol but were not doubly refractile in polarized light. The usual reactions for fat with osmic acid and sudan III were negative. At times two corneal lamellas were separated, and the resulting space was filled with large granular cells of the same type. Rochat stated that these cells resembled the so-called foam cells which are present with cholesterol in atrophic or old hemorrhage-filled eyeballs. He concluded these cells were not to be considered the primary factor in the production of the defect in Bowman's membrane but were the reaction of the body to a deposit of lipid substances. He did note, however, scattered swollen corneal corpuscles containing granules but could not be certain whether or not these changes were of postmortem origin. None of the other glassy membranes of the eye showed

changes similar to those seen in and near Bowman's membrane.

#### REPORT OF CASES

The following study was made of the eyes of 3 patients who died with lipochondrodystrophy. The cases of 2 of these patients were included in a previous clinical report on this disease.<sup>5</sup> Dr Theodore Holstein of Boise, Idaho, furnished the specimen, together with the clinical history in the third case and gave us permission to report the case.

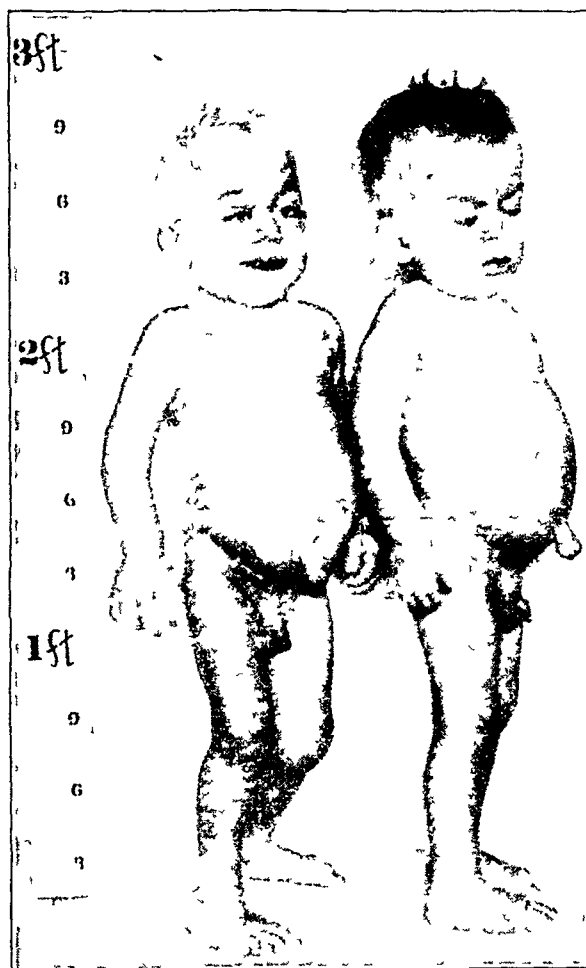


Fig 1—Patients in cases 1 and 2, showing typical changes of lipochondrodystrophy.

#### CLINICAL DATA

**CASE 1**—J. P. P., a boy, born July 8, 1935, was first seen at the University of California Hospital on Oct. 3, 1940 on admission to the clinic for study and observation.

**History**—He was a normal full term child at birth. There was no consanguinity in the family of either parent. The mother noted the appearance of lumbar kyphosis when the child was 5 months of age. The typical facies commenced to develop at the age of 1½ years, and by the age of 3 years the boy demonstrated most of the features of lipochondrodystrophy, with dwarfing, deformities of the extremities and corneal cloudiness.

<sup>2</sup> Berliner, M. L. Lipin Keratitis of Hurler's Syndrome (Gargoylism or Dysostosis Multiplex). Clinical and Pathologic Report, Arch Ophth 22 97 (July) 1939.

<sup>3</sup> Rochat, G. F. The Corneal Changes in Dysostosis Multiplex, Ophthalmologica 103 253, 1942.

<sup>4</sup> Waardenburg, P. J. Hurler's Dysostosis Multiplex, with Special Reference to the Ocular Symptoms, Ophthalmologica 99 307, 1940.

<sup>5</sup> Cordes, F. C., and Hogan, M. J. Dysostosis Multiplex (Hurler's Disease, Lipochondrodysplasia, Gargoylism), Arch Ophth 27 637 (April) 1942.

*Examination*—The appearance of the child was typical of lipochondrodystrophy. The head was large, and the face showed wide-set, protuberant eyes. There was a saddle nose, and the lips and tongue were thickened. He was almost deaf. There were protuberance of the abdomen, umbilical hernia and enlargement of the liver and spleen.

*Ocular Examination*—There was esotropia of the left eye of 10 degrees. Visual acuity could not be determined. Each cornea measured 13 mm in diameter. A uniform haze was seen in each cornea, without any

Autopsy showed pulmonary tuberculosis as the primary cause of death. The pathologist excised both corneas, placed them in a 10 per cent concentration of solution of formaldehyde U S P and forwarded them to the department of ocular pathology of the University of California Hospital.

CASE 2—D P, a boy, born Feb 13, 1937, a brother of the patient in case 1, was also first seen at the University of California Hospital on Oct 3, 1940 on admission to the clinic for study and observation.

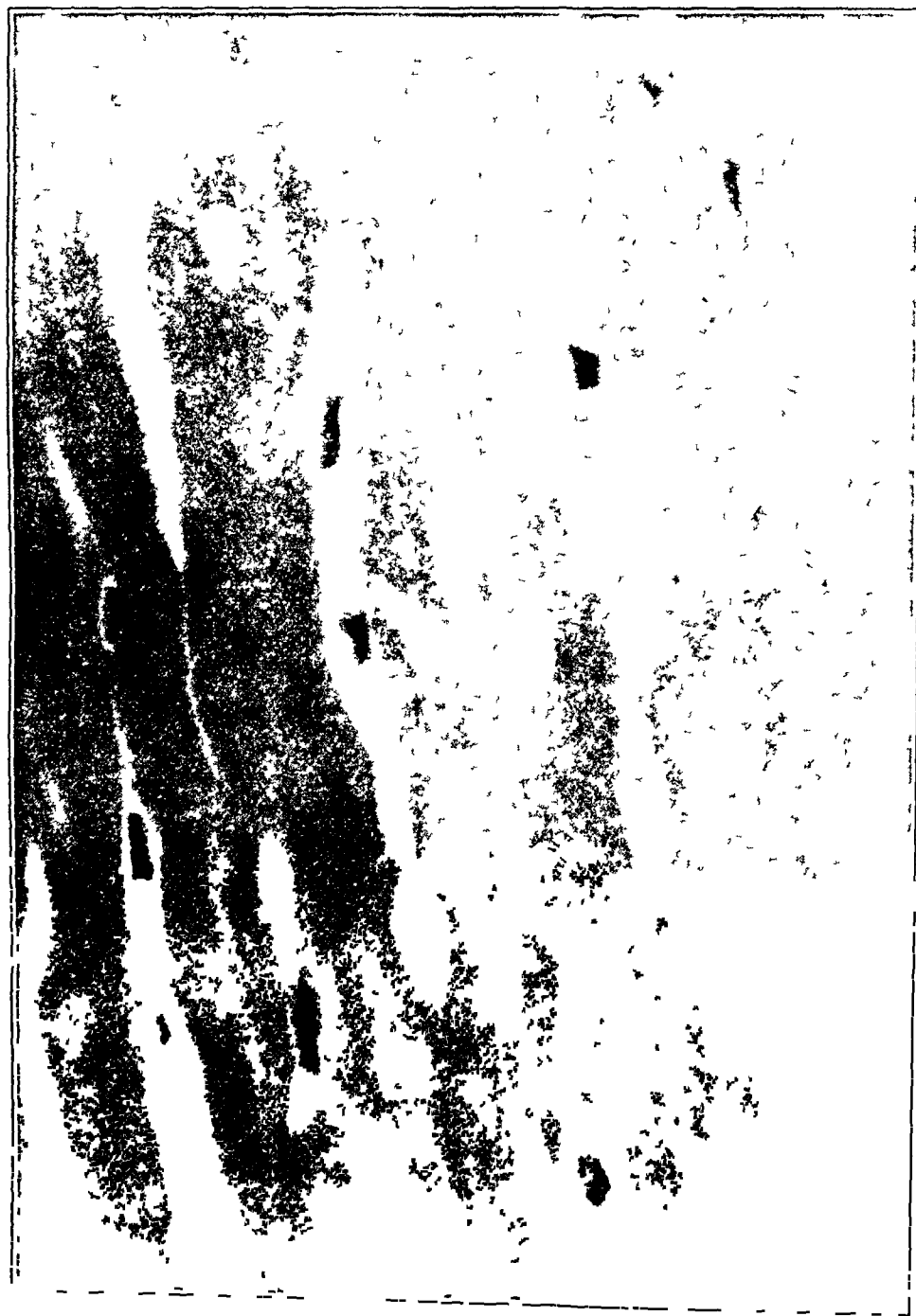


Fig 2 (case 1)—Frozen section, showing swollen, granular corneal corpuscles. High power lens, hematoxylin and eosin stain.

sign of ocular inflammation or tendency to corneal vascularization. Examination with the slit lamp showed a uniform distribution of gray punctate spots throughout the corneal stroma. The intraocular tension could not be obtained with the tonometer but seemed normal on palpation.

*Course*—The patient was observed in the clinic for some time and was then committed to the Sonoma State Home. He died there Feb 1, 1942, at the age of 6½ years.

*History*—The patient was a dissimilar twin, whose sister developed normally. The first signs of the disease appeared at the age of 5 months, when lumbar kyphosis was noted. At 1 year of age the head was enlarged, and the hands were broad and thick, with flexed, stiffened fingers. The general similarity to his older brother was notable at this time. He presented the complete syndrome of lipochondrodystrophy at the age of 3 years, and his development was much retarded. He could not talk at that time.



*Examination*—All the classic features of lipo-chondrodystrophy were present. The head was large, with prominent frontal bosses. The eyes were wide set and protuberant, and there was a saddle nose. The abdomen was protuberant and showed a large umbilical hernia. Palpation revealed an enlarged liver and spleen. There was pronounced dorsolumbar kyphosis.

*Ocular Examination*—There was mild exophthalmos. Visual acuity did not seem to be impaired, and palpation showed normal intraocular tension. The cornea of each

respiratory tract about two months after his older brother, at the age of 5 years. The corneas were removed at autopsy, fixed in a 10 per cent concentration of solution of formaldehyde U S P and forwarded to the department of ocular pathology.

CASE 3—R S, a boy aged 5 years, an only child, was first brought to Dr Theodore Holstein, of Boise, Idaho, in the early part of 1942 because the parents thought the child was blind. The peculiar features of lipo-chondrodystrophy appeared during the first year of



Fig 3 (case 1)—Paraffin section, showing thinning of Bowman's membrane and cellular infiltration. Low power lens.

eye measured 13.5 mm in diameter. Examination of the corneas with oblique illumination showed them to be fairly opaque, like ground glass. Examination with the slit lamp revealed the typical grayish punctate dots scattered throughout the stroma of the cornea, but more conspicuous in the deeper layers. Roentgenographic examination showed most of the typical features of lipo-chondrodystrophy.

*Course*—The patient was observed, likewise, in the clinic for a period and was subsequently committed to the Sonoma State Home. He died of an infection of the

life, when the corneas gradually became cloudy. By the age of 2½ years the child had a large head, and the eyes were wide set and protuberant. The lips were thick, and he was a mouth breather, as a result of the saddle nose. The abdomen was considerably enlarged. He died April 11, 1942, at the age of 5 years, of hydrocephalus. The right eye was removed at autopsy, placed in a 10 per cent concentration of solution of formaldehyde U S P and sent to the department of ocular pathology.

## PATHOLOGIC STUDY

*Technic*—The specimens in cases 1 and 2 were sent to us from the Sonoma State Home. There was delay in fixation of the tissues, which accounted for the post-mortem changes seen in the slides. The corneas in cases 1 and 2 were fixed for forty-eight hours in 10 per cent concentration of solution of formaldehyde U S P, after which they were divided in three portions with sharp scissors. One portion was used for frozen sections, one was embedded in paraffin, and the third

portion was used for paraffin sections, and the remainder of the eye was embedded in pyroxylin and cut in the usual manner. The stains used on this eye were the same as those employed in cases 1 and 2.

Chemical analyses for fats and fatlike substances were not made because the tissue had been fixed in a solution of formaldehyde and was therefore not considered suitable.

*Observations*—Cases 1 and 2. The changes in the corneas in these cases were similar, so they will be

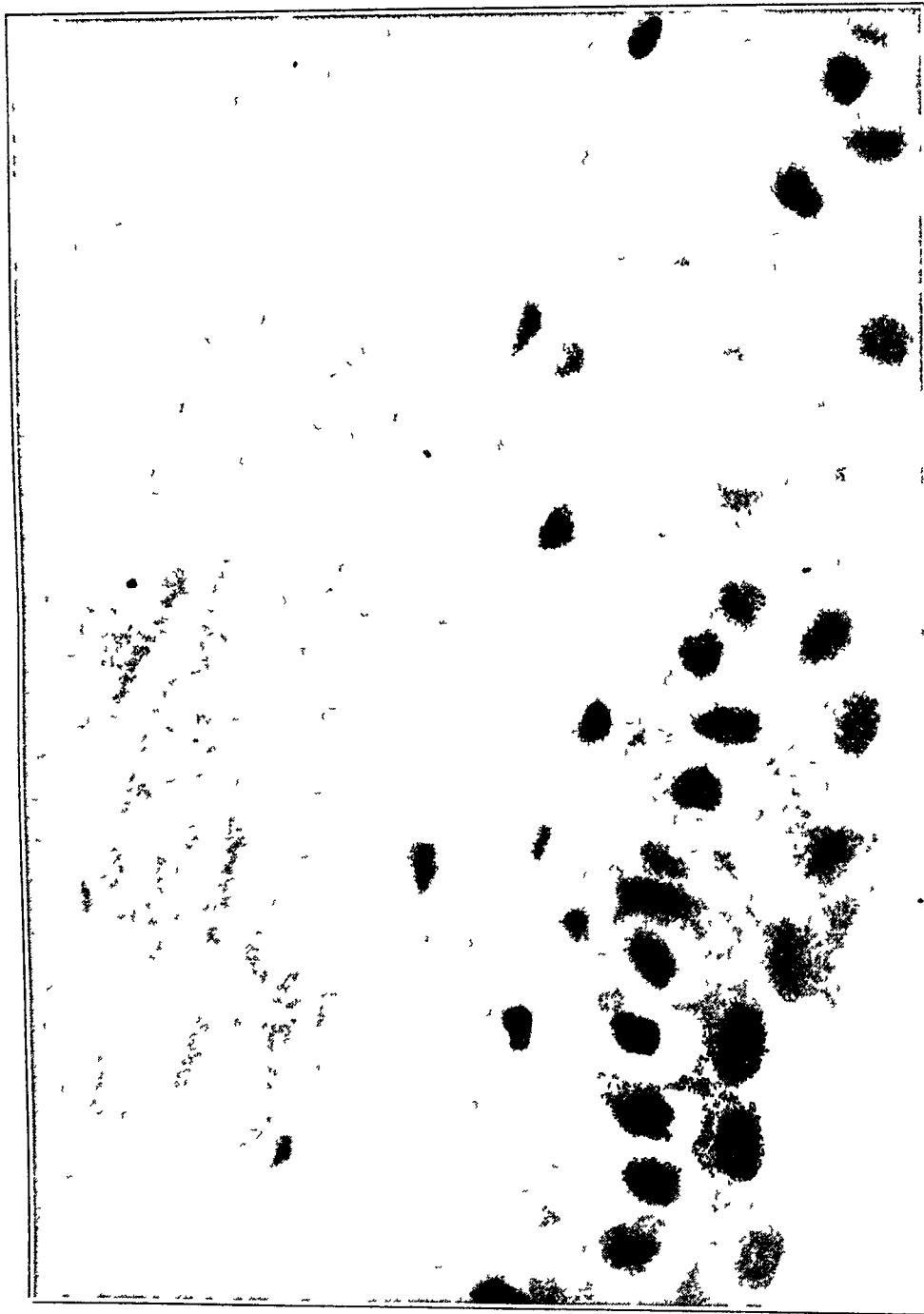


Fig. 4 (case 1)—Complete replacement of Bowman's membrane by the large cells. High power lens.

was embedded in pyroxylin. The portion which was used for frozen sections was cut in the usual manner, and the sections were stained in a variety of ways for neutral fats and lipids, as well as by the usual hematoxylin and eosin method. Routine preparations with hematoxylin and eosin and with the Masson stain were made of the sections embedded in paraffin and pyroxylin.

The eyeball in case 3 was already well fixed in solution of formaldehyde U S P on arrival. Large calottes were cut from the superior and inferior portions. The cornea attached to the calottes was excised, and a portion was used for frozen sections. Another

described together. Postmortem changes were evident throughout the cornea, but not to a notable degree. The epithelium was missing in some areas and partially desquamated in others, but that which remained was normal. The endothelial cells were also missing in some areas, but when present they seemed normal.

The principal changes encountered in the corneas were in the region of Bowman's membrane and in the corneal corpuscles. Most striking were the changes near and in Bowman's membrane. A great number of large polygonal or rounded cells were dispersed beneath this membrane across the whole cornea. In some areas,



where the infiltration of cells was pronounced, Bowman's membrane had become considerably thinned. There were numerous breaks in the membrane, and these dehiscences were filled with cells. The cells had an abundant, granular cytoplasm, and the nuclei were often eccentric. The granules in the cytoplasm were fine and stained darkly with hematoxylin. In frozen sections the granules were abundant throughout the cytoplasm, but in paraffin and pyroxylin sections they were almost entirely absent. The cytoplasm appeared vacuolated or honeycombed in the latter preparations,

technics for embedding in paraffin and pyroxylin, and it remained in the frozen sections. Stains for fat gave negative results in the corpuscles.

One might consider that part of these changes in the corpuscles were due to postmortem degeneration, but we have not observed such conspicuous alterations in other eyes which were fixed late.

CASE 3—Gross examination of the eye showed that it was of normal shape. The cornea was diffusely cloudy and measured 12 mm in diameter. The globe measured 24 mm in length, 25 mm in the horizontal



Fig 5 (case 2)—Swollen corneal corpuscles. High power lens.

the picture being similar to that observed after phagocytic cells lose their fat on being treated with solvents. Frozen sections prepared with sudan IV and other stains for lipids showed that these granules did not accept fat stains.

Of next greatest interest were the changes in the corneal corpuscles. The corpuscles and their processes were considerably swollen. The cytoplasm of the cells and processes contained a large amount of fine granular material, similar to that seen in the cells near Bowman's membrane. This material, too, was partially removed from the cell when the tissues were treated by the usual

diameter and 25 mm in the vertical diameter. Calottes were cut from the superior and inferior portions. The intraocular contents appeared normal.

Microscopic examination showed the same corneal changes as those encountered in cases 1 and 2, but to a lesser degree. The area beneath Bowman's membrane revealed a considerable number of large phagocytic cells. Bowman's membrane itself was less affected, but a number of complete breaks in its structure were encountered, and these dehiscences were filled with phagocytes. The phagocytes all had an abundant cytoplasm, which in frozen sections appeared filled with fine

granules. These granules were almost completely dissolved out in the paraffin and pyroxylin sections. The granules failed to take any of the stains for fat. The corneal corpuscles were also affected, showing numerous granules in their cytoplasm, but the process seemed less diffuse than that in cases 1 and 2.

There were numerous phagocytes of considerable size in the lamellas near the periphery of Descemet's membrane. The phagocytes could also be seen in the anterior trabecular meshwork. The material in the cytoplasm of these cells reacted similarly to that in

membrane confirm the observations of Berliner and Rochat. In each case the infiltration of large phagocytic cells was noted beneath the membrane, and it was also seen that these cells contained an abundant cytoplasm which was filled with a fine granular material. Our observations confirm those of Rochat in that this granular material was dissolved out of the cytoplasm when the tissues were treated with fat sol-



Fig 6 (case 2)—Pyroxylin section, showing swollen corneal corpuscles and complete replacement of Bowman's membrane by histiocytes at this point. High power lens, hematoxylin and eosin stain.

the cytoplasm of the corneal phagocytes and corpuscles. Numerous phagocytes were also noted in the stroma and on the anterior surface of the iris.

All the remaining ocular structures were normal except for the retinal and the optic nerve, which were atrophic. This change was considered secondary to the hydrocephalus.

#### COMMENT

From a histologic point of view, the corneal changes encountered in the region of Bowman's

vents. In none of the reports is there evidence that the material in the cells was of a fatty nature. Berliner and Rochat commented that stains for fat gave negative results, and we were unable to stain the material in any of our sections.

Sections of tissues from our 3 cases were sent to other pathologists for comment. Dr. Georgiana Theobald noted the infiltration of phagocytic cells in the region of Bowman's mem-

brane but stated that one should not assume that the material in the cells was of fatty nature. Dr L. von Sallmann made the following comment:

The sections in these cases show the same vacuolated cells in the superficial layers of the cornea, with partial replacement of Bowman's membrane, as were described by Berliner and Rochat. However, they present much more postmortem change than did Berliner's sections. The granular deposits in the stromal cells of the cornea

There is considerable evidence that the corneal corpuscles are involved in this disease. Both Berliner and Rochat noted that these corpuscles contained a granular material. Berliner was sure of its presence, but Rochat could not be certain whether or not it was a postmortem change. Our observations seem to indicate that there is actually an infiltration of the corpuscles.

The nature of this material in the cells is undetermined. Six autopsy reports are available

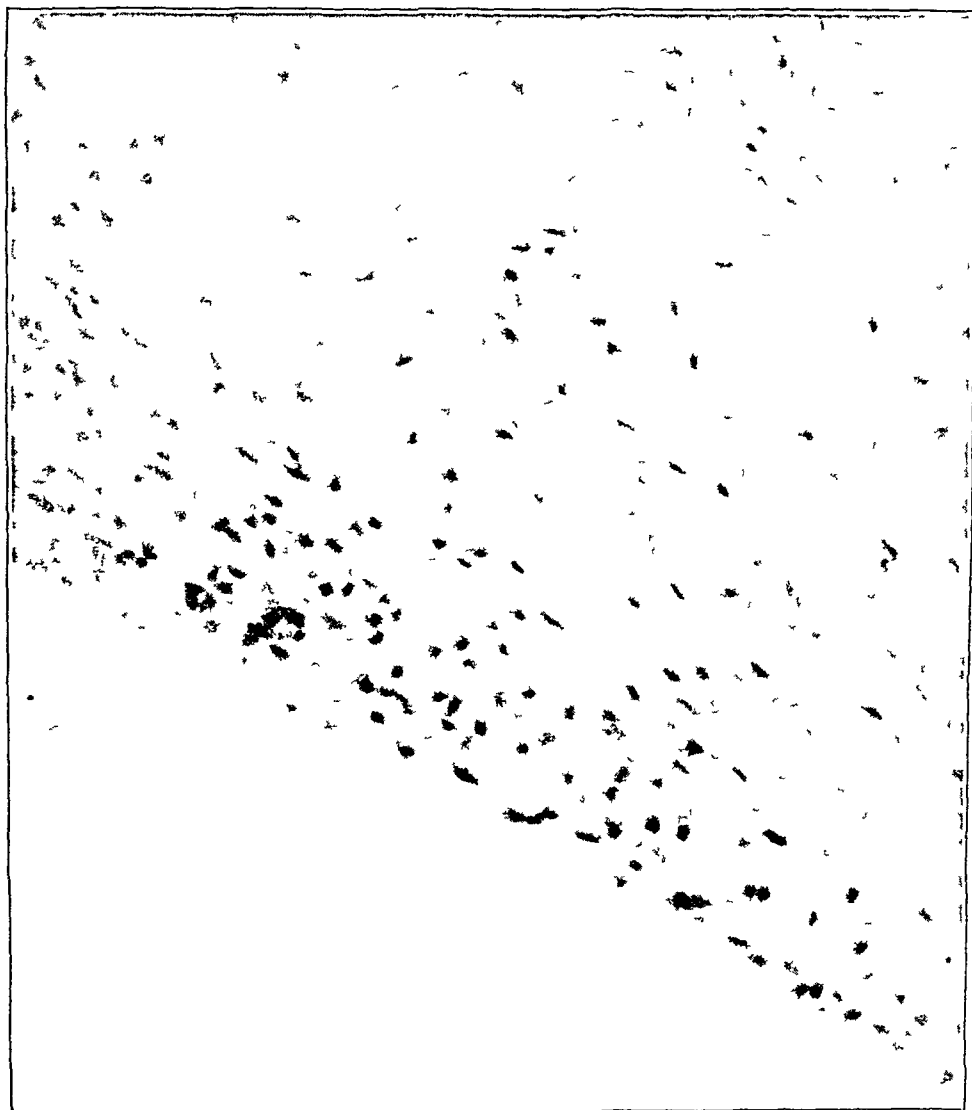


Fig 7 (case 3)—Pyroxylin section, showing cellular infiltration in the trabecular area near the end of Descemet's membrane. Low power lens, hematoxylin and eosin stain.

resembled those described by Berliner. The lipid nature of the granules is, I think, not proved beyond doubt, even though it is assumed.

Dr. Alson Braley stated:

All the slides show considerable postmortem change, and the cells, especially the large phagocytic cells, are difficult to distinguish. According to the description by Berliner, the histologic picture of this disease is fairly typical, and in none of the cases of lipochondrodystrophy so far described have the phagocytes in the cornea given a positive stain for neutral fat. It is possible of course that this material is lipid in nature.

for study. In almost all the cases the brain, pituitary, thyroid, testis, liver, spleen, endocardium, adrenal glands, osteoblasts and endosteal cells were reported to be infiltrated with a foreign material. The normal tissue cells seem to imbibe the material in most instances and become greatly swollen, with a granular cytoplasm. In this respect lipochondrodystrophy differs from the other lipodystrophies in that the fatty substances in the latter (Hand-Christian-Schuller, Niemann-Pick and Gaucher disease)

are present in the tissues in phagocytic cells. Our observations on the eyes in the present cases indicate that the substance in the tissues of patients with lipochondrodystrophy is present in phagocytes, in addition to the normal tissue cells. Examination of the other organs of the body in cases 1 and 2 confirms most previous pathologic studies. In the absence of chemical studies on the tissues in this disease, it is necessary to assume that the foreign material in the tissues is of fatty nature, even though it does not react to the usual stains for fat.

Correlation of the clinical data and the pathologic changes in the corneas in the present cases leads to the assumption that the numerous corneal opacities seen grossly and with the slit lamp are produced by the infiltration of phagocytic cells into the region of Bowman's membrane and by the swelling of the corneal corpuscles. There is no other cellular or fluid extravasation into the stroma to account for them.

#### CONCLUSIONS

In the pathologic examination of the eyes in 3 cases of lipochondrodystrophy, the corneal changes were found to be confined to the region of Bowman's membrane and to the corneal corpuscles.

The corneal opacities seen clinically are caused by (a) infiltration of numerous large phagocytic cells into the region of Bowman's membrane, causing thinning and ruptures in the membrane, and (b) swelling of the corneal corpuscles.

The phagocytic cells near Bowman's membrane and the corneal corpuscles show numerous fine granules in their cytoplasm. These granules are present in frozen sections but are removed by fat solvents, an indication of their possible lipid nature. The granules, however, do not take the usual stains for fat.

384 Post Street

# HEAT AND COLD IN THERAPY OF THE EYES

F H RODIN, M D

SAN FRANCISCO

Heat and cold have been used as therapeutic agents from time immemorial. Although they are universally employed in the treatment of various conditions of the eye, the difficulties and hazards of adapting them to oculotherapy have kept them from earning the popularity they deserve. Essential requirements are that the desired agent be readily obtainable, easily prepared and applicable with minimum discomfort and maximum benefit. To date no satisfactory simple method has been reported in the literature. The purpose of this paper is to present a procedure that has given gratifying results.

## HISTORY

Early in the history of medicine, Hippocrates (460 B C) wrote "Diseases of the eye are cured by drinking wine, or by baths, or by fomentation, or by bleeding, or by purifying medicines." These principles were adhered to by his followers until Celsus (25 A D) voiced a problem which even today has not been fully solved.

Concerning the application of fluid, the question is raised whether cold compresses are more appropriate than warm ones. In cases accompanied by pain, internal suppuration, itching, tears without running sores, warm compresses are more advantageous. In cases where there is only a slight amount of pain or where there is marked redness, cold compresses should be used.

Celsus advocated hourly application of compresses and the use of a small amount of water. At his instigation the sea sponge sometimes replaced the compress.

Treatment by steam or fumes is also of ancient origin. The Greek conception was to expose the open eyes to the vapor of a boiling eagle's liver until perspiration was induced. The Arabs preferred the steam from heads of sheep for the treatment of snow blindness, and fumes from the boiling flesh of wild donkeys was widely prescribed. The antiphlogistic properties of various plants in infusion and of resin from certain fruit trees were extolled in Galen's era (130 A D). A few of the more popular remedies of that time were rubbing the eye with substances such as

amber, gold, pearls and coral, ingestion of certain foods, baths, bleeding, and cupping. Turpentine and powdered cantharides were used as irritants, and extensive use was made of animal gall. Decoctions of lentils were supposed to act favorably on the lens, and lentil porridge and baked apples were employed as fomentations. Among the more curious remedies may be mentioned saliva, breast milk and powdered grasshoppers, while old beer and wine were utilized as vehicles, as well as butter, lard and honey (sixteenth century).

## HEAT

The effect of heat on certain ophthalmopathies, particularly when external, is twofold—analgesic and therapeutic. Heat is a vasodilator, producing increased hyperemia in inflamed tissues, which not only affords comfort to the patient but hastens the process of repair by accelerating metabolism and leukocytosis. It is recommended for mild keratitis, particularly of the phlyctenular type, mild blepharitis, acute conjunctivitis, corneal ulcer, and many intraocular disorders. In the preoperative care of patients with glaucoma it affords singular relief. It also plays an important role in the therapy of acute dacryocystitis and is beneficial in the treatment of acute glaucoma and of iridocyclitis, scleritis, episcleritis and other inflammations. In the case of conditions unidentified with pain, such as turbidity of the vitreous, intraocular hemorrhage and choroidal disease, it promotes recovery.

One of the readiest and most efficient agents is hot water, usually applied in the form of moist compresses. Hydrotherapy has encountered both favor and disfavor among ophthalmologists throughout the centuries, disfavor accruing in large part from the complicated systems in vogue. It was von Grafe<sup>1</sup> who revived the use of heat in modern times and enthusiastically advocated it as a curative measure. The literature abounds in descriptions of mechanical devices that have been recommended for this purpose, such as Leiter's coils, the Japanese hot box and specially

From the Department of Ophthalmology of Mount Zion Hospital, and the Division of Ophthalmology of Stanford University School of Medicine.

1 von Grafe, A. Anwendung lauer und warmer Überschlüge bei gewissen Ophthalmien, Arch f Ophth 6 133-150, 1860.

shaped water bags. Only a few of the less complicated methods will be reviewed here.

*Methods of Application*—Conner<sup>2</sup> fully described the use of hot water in the treatment of disturbances of the eyes and deplored the paucity of scientific literature on this form of therapy. He stressed the potency of hot water, unsupported by other measures, in promoting nutrition in tissues involved in a disease process, in removing causal organisms and in encouraging healing. He also went so far as to state that the reaction to heat of any pathologic condition of the eye was one of great improvement. Conner suggested that the patient bend his head over a bowl of hot water and throw the water gently with his hands over the affected eye without touching it. Since this method was rather tiring and the water could not be kept hot enough, he devised a pint-sized rubber bulb containing a thermometer, with an opening at the top to fit the patient's eye. A sustained even temperature was made possible by a stopcock-regulated flow of hot water through a tube attached to the top of the bulb and drainage of the cooled water from the bottom. Although the results were excellent, the apparatus was costly and unsuited to individual requirements, so it never came into general use.

Another ingenious method of using hot water described by Conner was to construct a clay dam on the patient's face while he was supine, so that when hot water was poured into the ocular cavity the eye was completely immersed. Thermometer readings enabled a constant temperature to be maintained, and drainage tubes disposed of the cooled water. The continuous, cautious supervision that this system demands has prevented it from becoming a routine procedure.

The third, and simplest, method recommended by Conner<sup>3</sup> provided direct contact with hot water by the medium of an ordinary water glass. A dam was produced by the rim of a filled glass held against the face and the side of the nose underneath the eye. With the head inclined forward the eye was completely submerged. The desired degree of heat could be maintained by replenishing the water in the glass. A further advantage was that antiseptics could be added if indicated.

Hotz, in discussing Conner's paper, stated that sensation informs the patient at what tempera-

ture the water is to be kept. He emphasized the efficacy of heat in reducing venous congestion of the anterior part of the eyeball, he claimed that the type of application was of secondary importance.

Wood<sup>4</sup> recommended the application of hot, moist compresses composed of strips of flannel or several thicknesses of gauze, wrung practically dry in water as hot as the eye could comfortably tolerate and changed the moment they began to cool. An alternative compress was a small towel or washcloth folded about 3 inches (7.5 cm) wide and 18 inches (45 cm) long. Holding one end in each hand, the patient dipped the cloth into water as hot as he could stand and applied it to the closed lids and the surrounding area. For best results the compresses were renewed every few minutes during the prescribed period.

Franke<sup>5</sup> offered the following technic of applying heat. Five to ten folds of bandage, or enough white linen or cotton material to cover the eye and vicinity, is soaked in the hot solution, the excess water is expressed gently, and the compress is applied to the closed eye. A compress of this type retains its heat only briefly, and as the aim of thermotherapy is to provide and maintain a fixed, unvarying temperature, additional compresses should be prepared for immediate replacement of the one removed.

The procedures for the use of hot compresses as described in textbooks for nurses are usually elaborate and consume considerable time in preparation and application. This is well illustrated by the method described by Denison and Eklund.<sup>6</sup>

**Equipment** The necessary equipment for the application of hot compresses is

Foment cup

Boric solution 1 50

2 wooden throat sticks

8-12 cotton balls

Boric ointment or vaseline [petrolatum] (to protect the skin)

Foment mat or small enamel tray

**Procedure** The boric solution, throat sticks, and cotton balls are placed in the foment cup and boiled for five minutes. The cup of hot solution is then placed on a protecting mat at the patient's table.

If there is any discharge, the nurse should wash off the patient's eye with warm boric solution and then,

4 Wood, C. A. *A System of Ophthalmic Therapeutics*, Chicago, Cleveland Press, 1909, pp. 81 and 84.

5 Franke, E. *Ocular Therapeutics: A Manual for the Student and the Practitioner*, St. Louis, C. V. Mosby Company, 1925, pp. 98-100.

6 Denison, A.-H., and Eklund, L. *A Textbook of Eye, Ear, Nose and Throat Nursing*, ed. 2, New York, The Macmillan Company, 1937, pp. 123 and 124.

2 Conner, L. Use of Hot Water in Local Treatment of Diseases of the Eye, *Am J M Sc* 82:466-472, 1881.

3 Conner, L. Hot Water in Management of Eye Diseases. Some Suggestions, *Tr Internat M Cong* 3:673-681, 1887.

with a throat stick, apply a thin film of boric or some form of ointment to the lids and surrounding area to protect the skin

The nurse should apply the fomentations on all children and old, feeble individuals. With the latter exceptions, intelligent patients may be taught to do this procedure very satisfactorily.

The patient is instructed to lift one cotton ball from the container with the throat stick and to squeeze out the solution with the blade of the other boiled throat stick. The steaming, moist pledget is held near the eye until it can be tolerated directly on the lid. Each cotton ball is discarded after use. The duration of the treatment is approximately eight minutes; for usually after this, the solution is not sufficiently hot to be effective. If prolonged application is required, the solution must be reheated at intervals. For constant hot applications, an electric stove plugged in at the bedside is very convenient.

From the preceding description it is evident that the methods recommended are cumbersome, require special equipment and are not altogether safe.

#### COLD

Cold, like heat, has a twofold effect—analgesic and therapeutic. Cold is a vasoconstrictor, producing anemia in chemotic and congested tissues, an action which is soothing to the patient and accelerates the process of repair. Cold applications lack the popularity enjoyed by hot ones, probably because less is known of the specific indications for their use and of their therapeutic effects, and because of the distaste frequently displayed toward them by patients. Nevertheless, they hold an important place in oculotherapy and are recommended for the relief of lesions produced by physical or chemical trauma, early conjunctivitis, blepharitis and acute trachoma and for postoperative care.

*Methods of Application*—Wood suggested the application of iced compresses made of seven or eight thicknesses of gauze or of absorbent cotton about  $2\frac{1}{2}$  inches (6 cm) in diameter. The flat, smooth surface of a block of ice was covered with six of these pads. When thoroughly saturated, they were wrung out as needed and applied to the eye. Ice water running down the face is unpleasant and may be avoided by careful removal of all excess water before application of the compress. Frequent changes were advised, as the inflammation rapidly imparts heat to the pad. Replacements were made with as brief an exposure of the affected area as possible. Wood recommended the folded towel compress dipped in a basin of cold or ice water for cold therapy. He advised a shorter period of application and a longer interval between applications and immediate discontinuation or replacement by hot

fomentations if the cold compresses caused pain or discomfort. He never used an ice pack.

Franke<sup>5</sup> recommended ice packs secured to the bed post so that their weight would not lie on the eye. He suggested that a towel be placed between the bag and the skin if it was desired to reduce the action of the cold. Berens<sup>7</sup> strongly warned against direct application of ice to the eye because of its swift destructive effect on the epithelial circulation.

Gifford<sup>8</sup> described a practical method of applying cold used by Dr. Loyal Davis in neurosurgical cases at the Passavant Hospital, Chicago. A flexible bag was made of a thin rubber glove with tied-off fingers and filled with shaved ice. The bag was applied to the closed lids over a layer of gauze. No evidence of delayed healing or damaged corneal nutrition was observed, but the relief of pain and chemosis was often remarkable.

#### TEMPERATURE AND TISSUE CONDUCTIVITY

Von Michel<sup>9</sup> was the first investigator to measure the temperature and the tissue conductivity at different levels of the eyeballs of rabbits. He made the puncture to the desired depth with an atraumatic, needle-shaped electrode equipped with a thermometer; the opposite electrode was immersed in water at a constant temperature. As compared with the average body temperature of the rabbits (38.5 to 38.9 C [101.3 to 102 F]), the galvanometric reading for the center of the anterior chamber was 31.9 C (89.42 F) and that for the vitreous, 36.1 C (97 F). Results recorded by different authors vary within a limited range.<sup>10</sup> After studies with a similar apparatus, Giese<sup>11</sup> affirmed that, with 2 exceptions, each of a series of infected eyes displayed an elevation in temperature of the conjunctiva, the average temperatures for the conditions studied being as follows: blepharoconjunctivitis 36.07 C (96.89 F), catarrhal conjunctivitis 36.87 C (98.3 F), corneal infiltration, 36.49 C (97.7 F), trachoma without pannus, 36.43 C

7 Berens, C. *The Eye and Its Diseases*, Philadelphia, W. B. Saunders Company, 1936, p. 1014.

8 Gifford, S. R. *Physical Therapy in Ophthalmologic Practice*, Arch. Ophth. 19:171-180 (Feb.) 1938.

9 von Michel. *Die Temperatur-Topographie des Auges*, Arch. f. Ophth. 32:227-232, 1886.

10 Comberg, W. *Auge und Allgemeinleiden, die physikalische Therapie*, in Schieck, F., and Bruckner, A. *Kurzes Handbuch der Ophthalmologie*, Berlin, Julius Springer, 1932, vol. 7, p. 692.

11 Giese, R. *Temperaturmessungen in Conjunctivalsack des Menschen*, Arch. f. Augenh. 28:292-304, 1895.

(97.5 F), acute iritis (1 case), 36.74 C (98.15 F), and panophthalmitis (3 cases), 36.56 C (97.8 F)

Application of iced compresses and ice bags to the eyes has been variously reported to cause a quick drop in the temperature of the conjunctiva of 1 to 15 degrees (C) (18 to 27 degrees [F]). Closing the lids brings a rapid rise of 2 to 3 degrees (C) (3.6 to 5.4 degrees [F]). According to Giese, the ice bag gave results inferior to those produced by direct application of cold compresses and was particularly ineffectual when separated from the eye by a strip of gutta-percha. The value of changing the compresses frequently was stressed by Hertel<sup>12</sup>, the optimal effect is obtained by replacement every thirty seconds. He asserted that his results were not influenced by diminished corneal circulation caused by the use of cocaine. Even compression of the carotid artery and subsequent anemia failed to reduce further the low temperature achieved by the use of ice water compresses. He therefore concluded that the thermoregulatory influence of the blood vessels during the application of hot or cold compresses is probably relatively small and that the action of the compresses is based not on changes in the state of the circulation but on conduction through the tissues. The response occurring in the deep layers he explained on the basis of the conductive power of the voluminous avascular eyeball. Iced compresses exerted a greater thermal effect than did hot compresses, and the action of cold was quicker and more lasting than that of heat.

#### METHODS OF APPLICATION

*Hot Compresses*—In observing the application of compresses to the eyes by nurses or by patients, one is impressed with the difficulty encountered in a treatment which should be simple and which has a beneficial effect on so many pathologic conditions of the eye. After having patients experiment with various types of compresses, I have found the following procedure for application of heat to be simple, safe and productive of minimum discomfort to the patient and of maximum benefit to the eye.

Preparation of the compress is as follows.

A wooden spoon is obtained (fig 1). This object forms a part of almost every household equipment or can be purchased in any five and ten cent store, in hardware shops and in some grocery stores. The bowl of the spoon is filled

with cotton, and cotton also is applied to the back of the spoon. A 2 inch (5 cm) gauze bandage is wrapped around the cotton in the form of a figure 8 and securely tied to prevent the cotton from falling out. Wide gauze can also be wrapped around the bowl and the cotton to form the compress. Hot water is poured into a small basin, and a medicament is added when prescribed. The compress is allowed to soak in the solution for a few minutes. It is then removed, the excess water is shaken off and it is applied to the eye (fig 2). As wood is a nonconductor of heat, the spoon handle re-

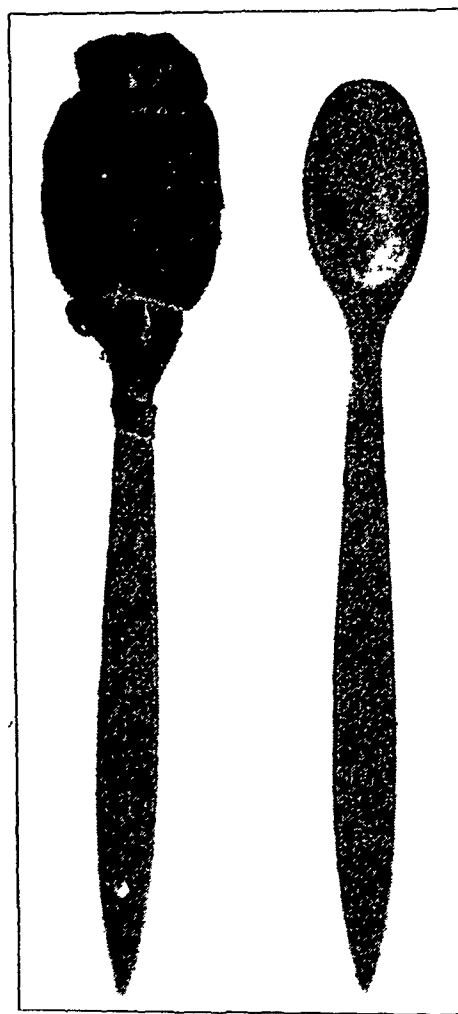


Fig 1—Wooden spoon and compress made by placing cotton in the bowl and on the back of a spoon. A gauze bandage or layers of gauze are wrapped around the spoon and tied.

mains cool, and the compress is easily handled and adjusted. The patient is the best judge of the proper temperature. As soon as the compress begins to cool, the bowl of the spoon containing it is introduced again into the basin for reheating and is again applied to the eye.

The duration and frequency of application are determined according to individual needs. Except with persons who are sensitive to heat or have a thin skin of the eyelids, application of a hot compress may be continued for fifteen minutes. The interval between applications de-

<sup>12</sup> Hertel, E. Wirkung von kalten und warmen Umschlagen auf die Temperatur des Auges, Arch f Ophth 49 125-167, 1899.



depends on the severity of the condition and the pain and discomfort associated with it. With severe disturbances, such as acute glaucoma and acute iridocyclitis, the compresses can be used every hour, and with milder ones, every three or four hours. A third consideration concerns the period over which application of the compress should be continued. This, again, depends on the type of the ophthalmic condition. In the case of a sty, it should be sustained until the sty points and is either opened or opens spontaneously and the inflammation has subsided, in cases of acute glaucoma and acute iridocyclitis, as long as pain persists and the condition of the eye demands. In cases of other conditions three or four days will suffice.



Fig 2—Spoon compress applied to the eye

I have been able to find only two references to this method of treatment in the literature. The first reference is by Parsons,<sup>13</sup> who stated

Much better than the usual hot fomentations is the method of hot bathing used at Moorfields Eye Hospital. A pad of cotton wool is tied into the bowl of a wooden spoon. The wool is dipped into a bowl of boiling water, and is then approximated to the closed eye. As soon as it has cooled sufficiently it is brought into contact with the closed lids. As soon as it ceases to feel hot, the wool is again dipped in the hot water and the process repeated. The bathing is continued for ten to fifteen minutes, and then a pad of dry warm cotton wool is bandaged over the eye. The hot bathings may be repeated frequently.

<sup>13</sup> Parsons, John H. *Diseases of the Eye*, ed 7, London, J & A Churchill, Ltd, 1934, p 660.

The second is a statement by Duke-Elder<sup>14</sup>

It may be given as repeated bathings with hot water, which is most easily carried out with the aid of a wooden spoon carrying cotton wool.

*Cold Compresses*—The simplest method of applying a cold compress is by placing cracked ice or ice cubes in a bowl of water. When the water is cold, cotton is dipped into the bowl, squeezed and applied to the eye. This can be repeated as soon as the cotton loses its frigidity. The procedure with the wooden spoon already described may also be employed. When ice is not available, tap water may be used. The water is allowed to run until cold. Cotton is held under the tap until a cold compress can be obtained and applied to the eye. As it is necessary to change the compress often, the tap water is allowed to run throughout the length of treatment.

Strips of gauze may be placed on ice cubes and then applied to the eyes.

An ice bag is sometimes recommended. This, as a rule, is not so satisfactory or efficient as a cold compress, because it is heavy and does not always properly cover the affected area.

#### COMMENT

Some patients obtain more relief from dry heat and others from moist heat, and it is occasionally a good plan to alternate the two. Certain patients seem to tolerate one form of thermal application better than the other, so that the decision whether to use heat or cold may often be determined largely by the patient's comfort.

#### SUMMARY

Heat and cold have been used in the treatment of ocular disorders from time immemorial.

Heat is a vasodilator, produces increased hyperemia and accelerates metabolism and leukocytosis. It is beneficial in the treatment of most inflammatory conditions, particularly of the anterior segment of the eyeball.

Cold is a vasoconstrictor, allaying pain and promoting healing by the production of anemia in the presence of chemosis and congestion.

My method of applying hot and cold compresses to the eye by means of moist cotton tied in the bowl of a wooden spoon with gauze has given gratifying results. The equipment is simple, safe and easily procurable.

The Columbia Foundation made this study possible.  
490 Post Street

<sup>14</sup> Duke-Elder, W S. *Text-Book of Ophthalmology*, St Louis, C V Mosby Company, 1941, vol 3, p 2210.

# BILATERAL METASTATIC UVEITIS ENDING IN PHTHISIS BULBI AS A COMPLICATION OF MEASLES

REPORT OF A CASE

LOUIS C RAVIN, M D

TOLEDO, OHIO

Ocular complications of measles, other than the almost invariably associated conjunctivitis, are rare<sup>1</sup> Metastatic uveitis as a complication of measles was mentioned by Duke-Elder<sup>2</sup> Optic neuritis,<sup>3</sup> retrobulbar neuritis with associated meningitis,<sup>4</sup> encephalitis with loss of vision<sup>5</sup> and severe retinitis<sup>6</sup> have also been reported as complications of measles

## REPORT OF A CASE

S T, a 3 year old girl, was first seen on Dec 18, 1943, for consultation, at the request of her physician The child had been admitted to the hospital after a severe episode of measles with associated bilateral otitis media and pneumonia Sulfathiazole therapy had been instituted three days previous to her admission Ocular examination revealed moderate lacrimation and photophobia, the conjunctivas were hyperemic The extraocular movements were well performed A slight ciliary injection was evident in both eyes, but no keratic precipitates were noted grossly Examination with a

hand loupe and a slit lamp was unsatisfactory, owing to lack of cooperation A slight turbidity of the aqueous could be detected The pupils measured approximately 3 mm in diameter They were round and regular but did not react to light either directly or consensually The irides lacked their normal luster After instillation of atropine sulfate solution, complete, annular posterior synechias were noted in both eyes, there was a dense pupillary membrane, through which neither the lens nor the vitreous could be seen The red reflex of the fundus could be detected around the periphery of the membrane Ocular tension was normal to palpation with the fingers

Drops of atropine sulfate solution were instilled every two hours, oral administration of sulfadiazine was ordered and dark glasses were put on During the patient's four weeks' stay in the hospital the ciliary injection cleared and the photophobia subsided The pupillary membrane became less dense Some large floating opacities could be detected in the vitreous, but no details were discernible at any time The fundus could not be seen There was no perception of light with either eye The vitreous gradually became opaque and finally developed into a pseudogliomatous mass

The laboratory data revealed the following The hemoglobin content was 11 Gm, the red blood cell count was 3,870,000 and the white cell count, 6,650 The urine contained no sugar or albumin, many bacteria and a rare white blood corpuscle The blood level of sulfadiazine was maintained between 4.5 and 5 mg per hundred cubic centimeters A culture of the discharge from the external canal of the ear revealed gram-positive and gram-negative small rods

The patient has been observed regularly since her discharge from the hospital When last seen, on May 3, 1944, the vitreous was a large pseudogliomatous mass, through which the fundus could not be seen, the globes were soft and moderately shrunken There was no perception of light with either eye

1 Berens, C, Kerby, C E, and McKay, E C Causes of Blindness in Children Their Relation to Preventive Ophthalmology, J A M A **105** 1949 (Dec 14) 1935

2 Duke-Elder, S Text-Book of Ophthalmology, St Louis, C V Mosby Company, 1941, p 2149

3 Russo, A Optic Neuritis from Measles, Boll d'ocul **16** 276, 1937, abstracted, Am J Ophth **21** 98, 1938

4 Dabney, S G Blindness Following Measles, Kentucky M J **30** 275, 1932

5 Heath, P Measles Encephalitis, Am J Ophth **15** 130, 1932

6 Shlossberg, F R, and Prizer, M Retinal Changes with Marked Impairment on Vision in Measles, Am J Ophth **23** 998, 1940

# BINOCULAR ORTHOPTIC TRAINING FOR AMBLYOPIC PATIENTS

KENNETH C SWAN, MD

PORTLAND, ORE

AND

ELSIE LAUGHLIN

IOWA CITY

A review of the literature reveals that for many years visual acuity of 6/15 or 6/12 in both eyes has generally been accepted as a minimal requirement for orthoptic training. In view of recent developments in orthoptic methods and also because maximal visual acuity of 6/15 or less in one eye is common with neglected concomitant strabismus, reconsideration of the minimal visual acuity requirement is indicated.

Visual acuity of 6/15 or better is dependent on foveal function, however, persons with small central scotomas frequently have single binocular vision. Also it is generally accepted that the peripheral fields of vision play a predominant role in fusional movements. For these reasons no one doubts that singular binocular vision may exist without foveal function in one or both eyes. Rather, the premise that visual acuity of 6/15 or better is necessary for orthoptics seems based on the belief that foveal fixation is essential for accurate objective adjustment of orthoptic instruments and that complex stereoscopic targets containing fine details are always best suited for the development of fusional movements.

It is important to adjust the orthoptic instrument to correspond exactly to the deviation of the eyes, particularly in the treatment of anomalous retinal correspondence, otherwise, the targets will not be visualized by normally corresponding points on the two retinas. For this purpose the cover test is used almost universally, that is, the targets are shifted in position until no movement of the eyes is apparent when the patient alternates fixation. This method is often unsatisfactory even when the patient is capable of foveal fixation in each eye. In persons with convergent strabismus, and particularly in persons with overaction of an inferior oblique muscle, it is not rare for the deviation to vary 10 to 20 prism diopters, depending on which eye is fixating. For such patients it is impossible to adjust the instrument so that the eyes do not change position as fixation is alternated. For

these patients and also for patients who are incapable of foveal fixation in one eye because of an absolute central scotoma, illuminated instruments such as the major amblyoscope are adjusted until the corneal reflexes are symmetric. In accuracy this method compares favorably with the cover test, providing the orthoptist accurately measures the angle gamma, the interpupillary distance and the distance of the eyes from the instrument. Therefore, it is not essential for the proper adjustments of instruments that both eyes be capable of foveal fixation.

Detailed targets exaggerating stereopsis stimulate fusional movements in patients with normal binocular vision, but in previously untreated squints the complexity and dissimilarity in the images of the two eyes are often confusing and favor alternation of fixation rather than fusion. Moreover, the fine details are not discerned by eyes with poor visual acuity. Targets consisting of simple colored disks subtending a visual angle of 1 to 3 degrees and lacking detailed points for foveal fixation are fused more readily. Patients with visual acuity as low as 6/60 in one eye are able to fuse these simple disk targets and acquire considerable amplitude of convergence and divergence provided that the extrafoveal fields of vision are relatively full and retinal correspondence is normal.

Development of single binocular vision is possible even when the patient has an absolute central scotoma in the afflicted eye, as is common in neglected monocular strabismus. In such patients with visual acuity of from 3/60 to 5/60 a large green ring with a central dot for fixation is presented to the normal eye, while a red ring with a blank background is presented to the amblyopic eye. To be visualized by the amblyopic eye the ring must subtend a visual angle larger than the scotoma.<sup>1</sup> Rings with a diameter

<sup>1</sup> From the Department of Ophthalmology, College of Medicine, State University of Iowa, Iowa City, Iowa

1 Red and green targets are projected on a white background, and filters are placed before the patient's eyes, so that he visualizes only the red target with one eye and only the green with the other eye. The scotoma is plotted with the better eye fixating.

subtending a visual angle of 5 degrees and with a rim wide enough to subtend an angle of 15 to 30 minutes suffice for most cases. The rings are colored to permit the patient to distinguish between the images of the two eyes. The colors are so balanced that the rings appear gray or black when fused but bright red and green otherwise. The illumination and contrast must be carefully controlled to minimize after-images and prevent retinal rivalry. Initially these targets are used with an instrument such as the major amblyoscope, which may be adjusted by the corneal reflex method to correspond to the deviation of the eyes, for it is imperative that the rings be visualized by normally corresponding retinal areas. When normal retinal correspondence is well established, rings printed on cards are used for home training with a simple prism stereoscope. With training many patients lacking sharp central vision in one eye fuse the rings and develop a considerable amplitude of fusional movements. Then single binocular vision becomes possible provided that the gross deviation of the eyes has been corrected by surgical intervention or by glasses.

When the better eye is occluded the squinting eye with an absolute central scotoma often fixates with an extramacular area, usually just adjacent to the nerve head. This point of eccentric fixation often has a visual direction corresponding to that of some point in the macular region of the usually fixating eye, that is, the patient has anomalous retinal correspondence. Until normal correspondence is established no attempt should be made to develop fusional movements by the use of ring targets. Rather, the ring targets should be used (repeated simultaneous stimulation of normally corresponding retinal areas) along with occlusion of the eccentrically

fixating eye<sup>2</sup> to establish normal correspondence. This method of treatment has established peripheral fusion in only 20 per cent of our patients with eccentric monocular fixation, but it is probable that a higher percentage of successes will result as experience is gained. The establishment of peripheral fusion provides assurance that the deviation will be permanently corrected. Also, in several patients who had only peripheral fusion initially there has been some return of central vision in the amblyopic eye over periods of two to four years. Formerly only cosmetic surgical repair could be offered to these patients.

#### SUMMARY AND CONCLUSIONS

The generally prevalent concept that visual acuity of 6/15 or better is essential for orthoptic training is no longer applicable. It is desirable that each eye be capable of focal fixation so that the cover test may be utilized for the adjustment of orthoptic instruments, however, adjustment of illuminated instruments so that the corneal reflexes are symmetric provides an accurate alternative method which may be used when one eye lacks sharp central vision. In patients with poor visual acuity due to a central scotoma training must be directed toward peripheral fusion. For this purpose orthoptic targets containing many fine details are of little value, but simple disk and ring targets subtending visual angles larger than the central scotoma are applicable. The development of peripheral fusion assures the patient of a permanent correction of the deviation and in some instances of a partial return of central vision in the amblyopic eye.

<sup>2</sup> Occlusion of the nonsquinting eye is harmful because eccentric fixation is stabilized by use. On the other hand, there is nothing to lose by occlusion of the squinting eye, for there is already an absolute scotoma which does not enlarge further.

# TOPOGRAPHIC AND ETIOLOGIC STUDY OF 1,176 INDIGENT BLIND PERSONS IN MASSACHUSETTS

A BASIS FOR PREVENTION OF BLINDNESS

HUGO B C RIEMER, M D

BOSTON

In the past the census enumerator has been depended on to supply information as to the number of blind persons. The enumeration at its best has been incomplete and often incorrect. This was definitely proved in the National Health Survey conducted by the United States Public Health Service from 1935 to 1936<sup>1</sup>

1 During the summer of 1930, the blind in a small Connecticut area were enumerated, one purpose being a comparison of results with those of the federal census. After thorough search it was found that not only was this special enumeration incomplete, but the Census Bureau had enumerated only 49 per cent of the blind in that area.

2 In the 1930 Census Bureau report, 626 blind persons were recorded for the State of Maine, yet in this State there were 1,268 persons receiving aid to the blind in April 1938, and it would not seem likely that all of the excess could be accounted for by difference in definition or by a real increase in the number of blind persons.

The census does not furnish authentic information as to the cause of blindness. This information, which is of utmost importance in the prevention of blindness, is now being obtained. The ophthalmologist considers a person blind when he no longer has perception of light, a condition known as amaurosis. The term blindness is now more inclusive. It includes that condition in which a person is considered to be economically blind, which actually means that he does not have sufficient sight for carrying on a gainful occupation.

Interest in the welfare of those handicapped by loss of vision has been greatly stimulated by the advent of the federal Social Security Act. This law was passed in 1935. In accordance with it the federal government makes provision for indigent blind persons by paying to the participating state one half of all payments up to \$40 a month. That is, if the state grants a person \$40 a month the federal government reimburses one half, or \$20. The state, by accepting the benefits of the provisions of this law, actually becomes a co-partner of the federal gov-

ernment in its operation. Since the federal government has assumed a part of the responsibility, it naturally follows that it will participate in carrying out the provisions of this law.

The federal government has promulgated certain regulations in order to make the law more universally applicable to all the states and to see that provision is made for equitable treatment and distribution of funds to all applicants for and recipients of financial assistance.

In order to facilitate its operation, the Social Security Board soon after the act became operable made certain definite recommendations relative to blindness.

1 It proposed a definition of economic blindness.

2 It required that certain medical data be collected and that they be kept by the state agency for each applicant for assistance, and, further, it suggested that the medical examination be made *only* by an ophthalmologist who holds a certificate from the American Board of Ophthalmology. This enables the state to have an authentic record of each person who applies for aid to the blind.

3 It developed a form of medical record covering certain medical data to be filled out by the ophthalmologist after his examination. Massachusetts used the suggested form until recently, when the Medical Advisory Committee and the director of the Division of the Blind composed a new form, which includes all the requirements set up by the Social Security Board but is developed in a way that best meets the need in Massachusetts. This form requires an accurate description of each eye and a statement as to the primary cause of blindness. The cause of blindness eventually will furnish authentic data, which can be used as the basis of a real program of prevention.

4 The board suggested the appointment of a trained ophthalmologist to review all medical reports.

Many of the states have appointed ophthalmologists to supervise their medical activities. It is the duty of the supervising ophthalmologist to review the medical report of each applicant.

<sup>1</sup> National Health Survey 1935-1936, Bulletin 10, United States Treasury Department, Public Health Service, 1938.

for relief because of blindness. If the report is incomplete or unsatisfactory a reexamination is required. When there is a doubt in the mind of the supervising ophthalmologist as to the facts reported, he can request that the applicant appear before him for examination. In some states medical reports on all blind persons requesting any type of service from the state department are required. In the state of New York medical forms for all blind persons who may become known to any public welfare department are filed with the Commission for the Blind. These are catalogued so that from this file studies of any one cause of blindness can be initiated.

Reliable statistics as to the prevalence of blindness are now being obtained. This has been accomplished by insisting on proper medical reports, as initiated by the Social Security Board. Even though these statistics represent only the number of needy blind persons, a truer picture of the causes of blindness in this country will be secured. One may even hope in a few years to obtain adequate information concerning the incidence of blindness.

The Massachusetts Division of the Blind, which is concerned chiefly with education and rehabilitation of blind persons and with the care of indigent blind persons, is now greatly concerned with a larger and more important program—prevention of blindness for all residents of Massachusetts.

This prevention of blindness program needs the full cooperation of all the members of the medical profession. This responsibility rests on them as well as with the ophthalmologists. How well physicians carry out the provisions of the laws which aim primarily to prevent blindness will be one of the most important factors in the prevention of blindness.

No one will argue that the use of prophylactic drops in the eyes of newborn infants has not reduced the incidence of blindness from ophthalmia neonatorum. Statistics have proved without a shadow of a doubt that this is true. Within the past year not a single baby who was blinded because of this disease has been reported to the Massachusetts Division of the Blind. It becomes more important than ever to be vigilant in cases of childbirth, since it is a well known fact that the incidence of venereal diseases increases in wartime. The law in Massachusetts requires a Wassermann or a Hinton test of pregnant women and provides for treatment of syphilis when present in the early stages of pregnancy, not only to benefit the mother but to prevent the birth of syphilitic offspring, who may later acquire interstitial keratitis, one of the important causes of blindness.

The law requiring a Wassermann or a Hinton test before marriage in Massachusetts has the same aim—to prevent syphilitic offspring, who may later become blind.

When it is realized that communicable diseases and trauma are two of the most important causes of blindness, I believe that there is complete agreement that something can be done to reduce the number of persons whose blindness is caused by one of these factors.

It is of interest to note that committees on conservation of vision have been appointed by state medical societies in the following states: Alabama, Connecticut, Florida, Indiana, Kansas, Maine, Missouri, Nebraska, New Hampshire, New Jersey, Oklahoma, Oregon, Pennsylvania, South Carolina and West Virginia. Special committees, concerned also with conservation of vision have been appointed by state medical societies in the following states: Delaware, Georgia, Iowa, Minnesota, New Hampshire, South Dakota, Tennessee and Wisconsin.

Plans are also under way for the publication of an article in the *West Virginia State Medical Journal* which will discuss (1) industrial accidents, (2) glaucoma, (3) ophthalmia neonatorum and (4) trachoma.

Data on the cases of 1,176 blind persons receiving aid for the blind in Massachusetts have been coded in accordance with the standard classification developed by the Committee on Statistics of the Blind. Table 1 gives these data on the basis of topography and type of disease.

It is interesting to note that of diseases which involve the eyeball glaucoma heads the list, with 111 cases, and myopia is second, with 100. In 38 cases blindness was caused by structural anomalies, such as albinism, anophthalmos, megalophthalmos, aniridia, coloboma and multiple structural anomalies.

In 187 cases blindness was due to disease involving the cornea, and in 114 of these it was due to ulcerative keratitis.

There were 100 cases in which blindness was caused by diseases of the iris and the ciliary body, in 78 of these it was due to iridocyclitis and uveitis and in 18 to sympathetic ophthalmia.

Disease involving the crystalline lens was responsible for blindness in 181 cases, not an unusually large number considering the age of the persons affected.

There were 217 cases in which involvement of the choroid and retina was responsible, in 60 of these the blindness was due to chorio-retinitis, in 59 to retinal degeneration, in 37 to retinal hemorrhage, in 29 to arteriosclerotic disease and in 25 to separated retina.

TABLE 1—*Classification of Blindness on the Basis of Topography and Type of Disease*

	No of Cases	Per Cent
<b>Eyeball in general</b>	275	24
Hypertension (glaucoma)	111	9 5
Refractive error (myopia)	100	8 5
Panophthalmitis and acute endophthalmitis	16	1 3
Structural anomalies	38	3 3
Degenerative changes	6	
Diseases of eyeball	4	
<b>Cornea</b>	187	16
Keratitis, interstitial	16	1 3
Keratitis, phlyctenular	1	
Keratitis, ulcerative	114	9 6
Pannus	10	0 9
Ulceration and vascularization	23	2
Other diseases of cornea	23	2
<b>Iris and ciliary body</b>	100	8 5
Iritis	1	
Iridocyclitis and uveitis	78	6 5
Keratolinitis	3	
Sympathetic ophthalmia	18	1 5
<b>Crystalline lens</b>	181	15
Cataract	179	15
Dislocated lens	2	
<b>Choroid and retina</b>	217	18
Choroiditis	3	
Retinitis	1	
Chorioretinitis	60	5
Detached retina	25	2
Retinal hemorrhage	37	3 3
Retinal degeneration	59	5
Arteriosclerotic disease of choroid and retina	29	2 5
Other diseases of choroid	3	
<b>Optic nerve visual pathway and cortical visual centers</b>	205	17
Optic nerve atrophy	145	12
Optic neuritis	14	1 2
Papilledema	5	
Neuroretinitis	4	
Retrobulbar and intracranial lesions	33	2 7
Other diseases	4	
<b>Miscellaneous and ill defined regions</b>	11	1
Amblyopia, undefined	11	1

TABLE 2—*Etiologic Classification of Blindness*

	No of Cases	Per Cent
<b>Infectious diseases</b>	376	32
Measles	1	
Meningitis	7	
Ophthalmia neonatorum	51	4 3
Gonorrheal	32	2 7
Type not specified	19	1 5
Scarlet fever	3	
Septicemia	5	
Syphilis	128	10
Prenatal	22	2
Acquired after birth	101	8 5
Origin not specified	5	
Trachoma	14	1 2
Tuberculosis	12	1
Other infectious diseases specified	5	
Infectious disease, not specified	150	12 8
<b>Trauma (including chemical burns)</b>	61	5 2
Nonoccupational activities	25	2
Occupational activities	25	2
Activities, not specified	11	1
<b>Poisoning</b>	13	1 1
<b>Neoplasm</b>	18	1 5
<b>General diseases (not elsewhere classified)</b>	93	7 9
Diabetes	45	3 8
Vascular diseases	40	3 4
All others	8	
<b>Diseases of prenatal origin (not elsewhere classified)</b>	152	13
Of hereditary origin established	5	
Of hereditary origin presumed	141	12
Of prenatal origin, cause not specified	6	
<b>Cause undetermined or not specified</b>	463	39
Unknown to science	348	30
Undetermined by physician	77	6 5
Not specified	38	3 3

Blindness was caused by disease involving the optic nerve and the visual pathway in 205 cases, in 144 of these it was due to atrophy of the optic nerve and in 33 to retrobulbar and intracranial lesions

Table 2 classifies the causes of blindness

Under infectious disease there are 376 cases, slightly over 31 per cent In 128 cases (about 11 per cent of the whole number) blindness was due to syphilis, and in 101 of these it was due to syphilis acquired after birth In 51 cases (about 4 5 per cent) it was caused by ophthalmia neonatorum, in 32 of these the ophthalmia was due to gonorrhea One hundred and fifty cases (almost 13 per cent) are classified under infectious diseases with the cause not specified

TABLE 3—*Age at Onset of Blindness*

	No of Persons in Age Groups	Per Cent of Total
<b>Total for all ages</b>	1,176	100 0
At birth	98	8 3
Under 1 year but not "premature" or "at birth"	46	3 9
1 year and under 10 years	124	10 5
10 years and under 20 years	75	6 4
20 years and under 30 years	96	8 2
30 years and under 40 years	139	11 8
40 years and under 50 years	190	16 2
50 years and under 60 years	186	15 7
60 years and under 70 years	129	11 0
70 years and under 80 years	58	4 9
80 years and over	16	1 4
Unknown	19	1 6

In 61 cases blindness was caused by trauma, including chemical burns In 25 of these it was due to nonoccupational activities and in 25 to occupational activities

In 13 cases blindness was due to poisonings and in 18 to neoplasms

Under general diseases there are 93 cases, in 45 of these the blindness was due to diabetes and in 40 to vascular disease

In 152 cases (practically 13 per cent) blindness was due to conditions of prenatal origin In 141 it was caused by retinitis pigmentosa of presumed hereditary origin In 5 cases the hereditary origin was established

The cause was undetermined or not specified in 463 cases, or practically 40 per cent In 348 cases (nearly 30 per cent), including cases of myopia, cataract and glaucoma, the cause was unknown to science In 77 cases the cause was not determined by a physician

Table 3 gives the age at the onset of blindness The largest number of persons, 186, or about 16 per cent, became blind between 50 and 60 years of age, and the next largest number, 139,



or about 12 per cent, between 30 and 40 years of age. There were 124, or 11 per cent, from 1 to 10 years of age. Ninety-nine persons had been blind since birth. The decrease in the number of persons between 70 and 80 years of age really begins with persons at the age of 65, when many recipients of aid prefer old age assistance to assistance because of blindness.

It has been shown by this statistical study that the causes of blindness in percentages correspond closely to those in other states in which a similar study has been made.

Brewster, of New Orleans, in a similar statistical study of 700 blind persons, made the optimistic statement that in 73 per cent of these persons blindness could have been prevented.<sup>2</sup> His statistics as to the percentage of the various causes of blindness correspond closely to mine.

A survey<sup>3</sup> in Indiana of 2,551 blind persons up to June 1938 gives as the causes of blindness

Infectious diseases	30.1%
Trachoma	9.6%
Syphilis	7.5%
Injuries	8.4%
Congenital and hereditary	8.3%
Noninfectious systemic diseases	7.4%

The director of the Division of the Blind in Massachusetts, with the cooperation of the Medical Advisory Committee, has had the following laws enacted in Massachusetts, which became effective in 1943:

First, an act relative to recording the treatment of infants at birth. This law requires the physician or a medical officer of the hospital to treat the eyes of an infant within two hours after birth with a prophylactic remedy furnished or approved by the Department of Health and to record on the birth certificate the use of such a prophylactic. Whoever violates this section shall be punished by a fine of not more than \$100. The principal change which this new law makes is that it requires the attending physician to record the use of the prophylactic on the birth certificate. Permissive legislation became effective in 1910, when the state furnished the prophylactic drops. The use of prophylactic drops was made mandatory in 1936.

Second, an act relative to reports of the treatment of certain wounds. This act classifies wounds caused by B. B. guns or other air rifles with the firearm or gunshot wounds which must be reported to the Commissioner of Public Safety or to the police authorities of the town.

Third, a law making it mandatory to report all cases in which vision is 20/200 or less in the

better eye or the peripheral field of vision has contracted to a radius of 10 degrees or less, regardless of visual acuity.

Prevention of blindness should be the chief interest of all official agencies for the blind and every other agency concerned with the welfare and the health of all persons. This program for prevention of blindness cannot succeed without the full cooperation of the entire medical profession. There are certain fundamentals on which such preventive measures must rest. These fundamentals are:

- 1 Adequate medical determination of blindness
- 2 Early contact with potentially blind persons
- 3 Ability to care for those who are potentially blind, whether adults or children in an adequate manner
- 4 Proper prenatal care
- 5 Proper liaison between official agencies for blind persons and other agencies, such as the health department, the public safety department, industrial commissions, labor commissions and the education department

Statistical studies of the causes of blindness form the basis of any real program of prevention. A broad program for the prevention of blindness requires the cooperation of local communities, philanthropic societies and physicians. When the causes are known, efforts at prevention can begin.

This study emphasizes the following needs:

- 1 Enforcement of all laws enacted for the control of infectious diseases
- 2 More care in reporting the cause of blindness
- 3 Early detection of all cases of glaucoma
- 4 Detection of diabetes before the devastating effects of this disease are manifest
- 5 Prevention of industrial and nonindustrial injuries
- 6 Authentic data on cases in which blindness is hereditary
- 7 Adequate measures to assure proper medical care for persons afflicted with disease or injury to prevent onset of blindness.

A new bill, the Barden-Lafollette Bill, Public Law 113, effective since July 6, 1943, aims to provide measures to rehabilitate all persons who are blind because of industrial injuries and others who can be restored by physical or medical means to a self-supporting status. These include blind persons in whom sufficient sight might be restored to allow a gainful occupation.

<sup>2</sup> Brewster, H. F. Causes of Blindness in Louisiana, New Orleans M. & S. J. 91 166-173 (Oct.) 1938.

<sup>3</sup> Kettler, J. R., and McCaslin, J. R. State and the Blind, J. Indiana M. A. 31 539-543 (Oct.) 1938.



# Ophthalmologic Reviews

EDITED BY DR FRANCIS HEED ADLER

## EPIDEMIC KERATOCONJUNCTIVITIS AND VIRUS DISEASES OF THE EYE

ANDREW RADOS, MD

NEWARK, N J

### VIRUS DISEASES WITH OCULAR COMPLICATIONS

Virus diseases and the closely related rickettsial infections may involve the eye secondarily. The complications of the virus group of diseases are so well known that it will suffice here merely to mention the varieties that may commonly affect the eye, such as measles, rubella, rabies, psittacosis, the common cold, influenza, encephalitis, lymphocytic choriomeningitis, poliomyelitis, Australian X type of encephalitis, louping ill, Rift Valley fever (enzootic hepatitis), yellow fever, pappatacci fever, dengue, vaccinia, mumps and lymphogranuloma venereum.

*Rare and Recent Forms*—In rare instances virus diseases affecting animals only may produce ocular complications in human beings. Babel<sup>1</sup> described a serofibrinous iritis accompanying pseudotuberculous meningitis (swineherd's disease) and cited Fatzer, who noted papillitis as a complication in his case. In Babel's case cultures of the aqueous inoculated into the anterior chamber of the eye of the rat, mouse and guinea pig gave negative results.

One of the diseases with which ophthalmic symptoms most commonly occur is encephalitis. The ocular complications of encephalitis were analyzed by Kennedy<sup>2</sup> as due either to obliteration of normal function or to release of functions normally controlled by centers higher in the brain. The most usual complications were ptosis with associated weakness, paralysis of both external rectus muscles, combined paresis of the third and sixth nerves, divergence paralysis and blepharospasm, due to the downpouring of tonic impulses from the basal ganglia when freed of their normal cortical control.

Read at a meeting of the Academy of Medicine of Northern New Jersey, Section of Diseases of the Eye, Ear, Nose and Throat, Newark, N J, Oct 11, 1943.

1 Babel, J. Fibrinous Iritis in Patient with Swineherd Disease, *Ophthalmologica* **96** 159, 1938.

2 Kennedy, F. Ocular Disturbance in Epidemic Encephalitis, *J Nerv & Ment Dis* **69** 194, 1929.

Paralysis of the external rectus muscles is caused by the perivascular lymphocytic infiltration of the brain stem around the aqueduct. A lesion of the quadrigeminal plate manifests itself in the Parinaud syndrome, diminution or loss of vertical conjugate movements or interference with lateral conjugate action. Inequality of the pupils appears temporarily, with the Argyll Robertson phenomenon, usually bilateral paralysis of accommodation and various types of nystagmus, indicating involvement of Deiters' nucleus or the central vestibular connections. Furthermore, retrobulbar neuritis and papilledema may be produced by their widespread neurotrophic infection.

In the more recent, and generally less known literature it is worth while to note the complications of mumps. Danielson and Long<sup>3</sup> referred to 7 instances of unilateral keratitis, in addition to their own cases. Dacryoadenitis, scleritis, uveitis, retrobulbar neuritis, neuroretinitis and ocular palsies are known to be associated with epidemic parotitis. Packard<sup>4</sup> called attention to corneal involvement in cases of varicella and referred to a similar observation by Oppenheimer.

In his review, Bruce<sup>5</sup> gave a fair picture of ocular complications associated with the common virus diseases. Only lymphogranuloma venereum merits special mention, having been described as recently as 1913 by Durand, Nicôlas and Favre. The diagnosis of lymphogranuloma venereum was greatly facilitated by the specific cutaneous test of Frei. Von Haam and Hartwell<sup>6</sup> observed unilateral or bilateral conjunctivitis following intracerebral inoculation of the virus in mice,

3 Danielson, R W, and Long, J C. Keratitis Due to Mumps, *Am J Ophth* **24** 655, 1941.

4 Packard, R. Varicella of the Cornea, *Brit J Ophth* **20** 15, 1936.

5 Bruce, G M. Virus Diseases and the Eye in Childhood, *J Pediat* **18** 592, 1941.

6 Von Haam, E, and Hartwell, R. Experimental Conjunctivitis Caused by Virus of Lymphogranuloma Inguinale, *J Trop Med* **39** 190, 1936.

monkeys, ferrets, cats, sheep and calves. The development of a lesion was a positive sign of infection and was followed by fatal meningo-encephalitis. These authors observed only acute hemorrhagic or purulent conjunctivitis in cases of lymphogranuloma venereum. Weimer and his associates<sup>7</sup> presented the case of a Negro aged 32 with a lesion of the left upper lid, the site of an extragenital infection associated with lymphogranuloma venereum. Histologic study revealed large monocytes containing Donovan bodies.

Levaditi and his co-workers<sup>8</sup> described a case of the Parinaud syndrome with preauricular and submaxillary adenopathy. This observation was confirmed by the findings of Hashimoto and Tamata<sup>9</sup> in 3 cases and by the convincing description of the disease by Appelmans,<sup>10</sup> who followed the development of the Parinaud syndrome in a young woman, a laboratory worker. She had accidentally acquired the infection while working with the virus. In Meyer and Reber's<sup>11</sup> case the virus origin of a superficial, narrow, crescentic corneal ulcer in a patient with lymphogranuloma venereum of the rectum is questionable, for biopsy of the lesion or recovery of the virus, with confirmatory inoculation, was lacking.

An entirely new chapter in the knowledge of sequelae to virus diseases was opened by the observations of Gregg<sup>12</sup> and Swan and co-workers<sup>13</sup> on congenital abnormalities in infants whose mothers had contracted rubella while pregnant. This work is so recent that all the possible consequences of the infection cannot as yet be fully ascertained.

The first observation was furnished by Gregg, who described the cases of 78 infants with congenital cataract (62 with bilateral and 16 with

the unilateral type) whose mothers, with few exceptions, had had rubella in the early part of pregnancy. Forty-four infants simultaneously had a congenital lesion of the heart. The cataracts were of the dense nuclear variety. Eleven of the infants with monocular cataract had microphthalmia. Gregg emphasized that these cataracts had no similarity to any of the morphologic types of congenital and developmental opacities previously reported.

Based on the reports of Gregg, Swan and his associates made an exhaustive study of 49 women with rubella to whom 31 infants were born with congenital abnormalities. Of these 49 women, 35 were examined while they had the eruption; the remaining 14 (with 13 congenitally defective infants) failed to seek medical advice at the time of the alleged rash, and hence the clinical diagnosis could not be confirmed by medical examination. All but 2 of the 31 mothers with congenitally defective infants had rubella within the first three months of pregnancy. All the 25 patients who had rubella in the first two months of pregnancy gave birth to infants with congenital abnormalities. Of 8 women who had rubella in the third month of pregnancy, only 4 gave birth to defective offspring.

Of 14 infants with defective eyes, 13 (6 males and 7 females) had cataracts and 1 (a female) buphthalmos. With 2 exceptions, none of the mothers had been pregnant more than two months at the time of onset of the exanthem. Of the infants with cataract, 10 had bilateral and 3 unilateral involvement, and all the cataracts were of the central nuclear type. Two of the infants had nystagmus, 1, moderately severe microphthalmia, and another microphakia. One of the infants with bilateral cataract presented microphthalmia in one eye and small pigmented spots in the fundus of the other eye. The clinical appearance of the cataracts conformed to Gregg's description—a flattened, white, dense disk with six radiating lines, the latter presumably representing the superimposed anterior and posterior sutures. The lens appeared to be small, and in good mydriasis a clear peripheral zone was noted. On dissection, the capsule and the cataractous disk seemed to be adherent. Nine of the infants showed cardiac involvement, 3 mental deficiency, and 1, talipes equinovarus.

Of the infants with no involvement of the eyes, 7 were deaf-mutes, and 17 had cardiac lesions and microcephaly.

For the mothers whose infants had cataract, the average duration of pregnancy at the time of the appearance of the exanthem was one and a half months, while for the mothers of the deaf-mute children it was two and one-tenth months,

7 Weimer, A. L., Gaynon, I. E., and Osherwitz, M. S. Granuloma Inguinale of Eyelid. Report of Case, *Am J Ophth* 26 13, 1943.

8 Levaditi, C., Bollack, J., Basch, G., and Desvignes. Conjunctivitis with Adenopathy, Due to Virus of Nicolas-Favre's Disease, *Bull Soc franç de dermat et syph* 43 1238, 1936.

9 Hashimoto and Tamata. Paradenic Etiology of Parinaud's Conjunctivitis, *Sang* 12 85, 1938.

10 Appelmans. Parinaud's Conjunctivitis Caused by Virus of Nicolas Favre's Disease, *Bull Soc belge d'opht*, 1938, no 77, p 130, *Ophthalmologica* 96 321, 1938.

11 Meyer, G. P., and Reber, J. A Case of Corneal Ulcer Associated with Lymphogranuloma Venereum, *Am J Ophth* 24 161, 1941.

12 Gregg, M. N. Congenital Cataract Following German Measles in the Mother, *Tr Ophth Soc Australia* 3 35, 1941.

13 Swan, C., Tostevin, A. L., Moore, B., Mayo, H., and Black, G. H. Congenital Defects in Infants Following Infectious Diseases During Pregnancy, *M J Australia* 2 201, 1943.

evidence that the type of congenital defect is dependent on the stage of pregnancy at which the rubella occurs

The unusually large number of congenital defects following rubella in this series may have been due to an altered virulence of the virus. The embryonic cells are more susceptible to infectious agents than those of adult tissues. The young and the outgrown tissues are known to differ biologically in behavior toward certain agents. In this connection I should like to note that the lenses of young rabbits are more sensitive to irradiation than those of adult rabbits, consequently, a smaller dose will produce radiation cataracts. Furthermore, the same agent, radiation, produces retinal rosettes in the embryonic rabbit if the pregnant uterus is exposed to roentgen rays. In cases of rubella the virus penetrates the chorionic barrier and produces severe lesions in the embryonal tissues. It appears that the cells are highly susceptible only in the first three months of pregnancy, or it may be that after that period, the placenta being formed, the barrier between mother and fetus becomes impenetrable to the offending virus.

#### OCULAR COMPLICATIONS IN RICKETTSIAL INFECTION

The ocular complications of rickettsial disease were recently reviewed by Venable and Pollock<sup>14</sup>. These diseases are all insect borne and show the Weil-Felix reaction with *Proteus* X19 or *Proteus* XK, they usually confer long-lasting immunity. The rickettsias are minute bacillary or diplobacillary organisms. Like the viruses, the pathogenic rickettsias multiply outside the body only, in various kinds of tissue cultures, and develop intracellularly. The organism of typhus lies in the cytoplasm, and that of Rocky Mountain spotted fever often grows intranuclearly in tissue cultures. They show apparent selective affinity for certain types of cells. Though the rickettsias occur in all organs and in the blood, they accumulate visibly in cells of mesothelial origin, particularly in the lining cells of the large serous cavities of the body. The frequency of the presence of rickettsias in insects and their growth in tissue cultures at a temperature lower than that of the mammalian body suggest that they originally were insect parasites. Their characteristics of nonfiltrability, visibility and affinity for ordinary bacterial stains ally them with bacteria. In their staining reactions with special methods (Giemsa, Castenada and Machiavello), their growth in living cultures and their

intracellular position, as well as their affinity for mesothelial cells, the rickettsias show points in common with the viruses.

According to Pinkerton, the rickettsias are pleomorphic bacteria adapted to anthropod tissues. At present, they are considered to belong to an intermediate class between viruses and bacteria. They may eventually be included with the bacteria. Typhus (*Rickettsia prowazekii*) is transmitted by the louse or flea, Rocky Mountain spotted fever (*Rickettsia dermatitoxenus*), by ticks. In contrast to these diseases, boutonneuse fever and tsutsugamushi fever are similar in that there are local ulceration and adenopathy at the site of the tick bite. Trench fever, proved to be transmitted through the louse, is most probably also a rickettsial disease. Ocular complications are observed with typhus. Only mild conjunctivitis occurs with Rocky Mountain spotted fever. In cases of tsutsugamushi fever Nagayo and associates<sup>15</sup> observed severe inflammatory complications in the anterior segment of the eye. He produced the lesions by introducing infected material into the anterior chamber of the eye in rabbits, monkeys and guinea pigs. The infected eye acquired lasting immunity, and the endothelial cells of Descemet's membrane exhibited a large number of rickettsias.

#### CHARACTERISTICS OF VIRUSES

The genius of Pasteur anticipated that rabies is caused by an invisible organism smaller than bacteria, but the actual proof was furnished in 1892 through the transmission of the mosaic disease of the tobacco plant by cell-free filtrates (Swanovski and Beijerinck). The existence of such filtrable organisms was shortly confirmed by evidence that foot and mouth disease is similarly caused by invisible agents. The last two decades have brought an enormous amount of knowledge concerning the propensities of the agent, and numerous diseases belonging to the virus group have been discovered.

With the resolving power of the ordinary microscope and with the usual illumination the viruses in general are invisible. They pass through the pores of porcelain filters or collodion membranes of determinable porosity and are grown only in cultures of living tissues. Their cultivation in the presence of living, susceptible cells indicates their intimate relation to the host cell. The various viruses often adapt themselves to one or to a few animal or plant hosts or are

14 Venable, H. P., and Pollock, F. J. Rickettsias in Ophthalmology, Arch Ophth 30 362 (Sept) 1943

15 Nagayo, M., and others. Rickettsia Orientalis as Causative Agent of Tsutsugamushi Disease, Jap J Exper Med 9 87, 1931, Virus of Tsutsugamushi Fever, Compt rend Soc de biol 104 637, 1930

characterized by special affinity for a group of cells in the host, such as that of the herpes virus for ectodermal derivatives. The invaded cellular elements react typically to the virus with stimulation or destruction or with the formation of inclusion bodies. Immunity is often lasting (variola, varicella) but may be either transient (herpes simplex, common cold) or not demonstrable (trachoma, molluscum contagiosum).

A description of the exact nature of the viruses is unnecessary, in view of the excellent review by Thygeson.<sup>16</sup> It should be mentioned that the viruses show enormous range in size, even after one discounts the possible error in measuring the particles on which the virus was adsorbed. The scale varies from 150 or 250 millimicrons (in vaccinia and psittacosis) to 10 to 12 millimicrons (in poliomyelitis and aphthous stomatitis [foot and mouth disease]).

Through animal passage the properties of a virus may change, and adaptation occurs, resulting, for instance, in conversion of the smallpox virus into the vaccinia virus or into the yellow fever virus, with production of encephalitis in monkeys. The cell reacts to invasion of the virus with the formation of cytoplasmic or nuclear inclusions. Some of the inclusion bodies are characteristic enough (Negri bodies in rabies, and the bodies in molluscum contagiosum) to permit microscopic diagnosis of the disease in question. Their exact nature is still debated, but doubtless they express the influence of the virus on the cell. The inclusion bodies were regarded as indicating reactive inflammation or degeneration of the cell, or as being aggregates of the virus itself or particles of the virus enveloped by cellular material. The last concept led von Prowazek to designate them as chlamydozoa, or mantle animals. The inclusion bodies are not necessarily present in every virus disease; they are absent, for instance, in poliomyelitis. These bodies, being larger than the virus, necessarily contain cellular material too. Von Prowazek and Lipschutz,<sup>17</sup> the latter using the designation stronglyloplasm, concluded that the inclusion body was a microcolony of the virus. Lipschutz observed even brownian movements. The most recent investigations with microdissection of the inclusion, in which the body is dissolved by means of an alkaline solution of trypsin, seem to furnish further evidence of a hyaline-like matrix and minute particles.

The matrix is the product of the cell reaction and varies in chemical constitution with the specific virus.

Serum obtained from patients after recovery from the disease neutralizes the homologous virus. The presence of complement fixation, precipitation and agglutination antibodies testifies to the active antigenic nature of the viruses, with specific properties. The presence of virus-neutralizing antibodies is utilized in neutralization tests for diagnostic purposes. The serum, after being mixed with the virus, is inoculated into susceptible animals. The presence of complement fixation antibodies in convalescent serums is one of the most conclusive evidences of the presence of the virus, especially since these antibodies are absent in the acute stage. The neutralization tests are of great diagnostic significance in cases of such diseases as encephalitis, poliomyelitis, psittacosis, herpes and epidemic keratoconjunctivitis. The neutralizing antibody test, however, has limitations, since a typical attack may fail to develop, or, on the other hand, the disease may occur in persons already possessing antibodies in their serum.

The exact nature of the viruses is still debated. A bacterial origin is generally considered improbable. According to the fundamental attributes of life, namely, reproduction and adaptation, the viruses are living organisms. They have antigenic properties and show the faculty of adaptation in response to different environments. But all these properties are linked by the association of the virus with living cells, either in the body of the host or in cultures containing living cells. Actual proof of the living nature of viruses—cultivation without the presence of living cells—has not been obtained.

Many investigators consider the viruses as autocatalytic, enzyme-like agents and believe that their minute size, for example that of the virus of poliomyelitis, as shown by differential filtration and ultracentrifugation, precludes the possibility of their being living things. The discovery by Stanley of the crystalline form of the virus of tobacco mosaic disease, confirmed by other investigators, seems to prove that viruses are not animate organisms. But in Pirie's opinion, crystallinity denotes a structural regularity only, and not incompatibility to a living state.

The enormous progress in the study of virus disease in the past two decades has taught that demonstration and identification may be accomplished by the use of susceptible animals and chick embryos. After the virus is recovered, it is identified by determination of the susceptible

<sup>16</sup> Thygeson, P. Viruses and Virus Diseases of the Eye, Arch. Ophth. **29** 285 (Feb.), 488 (March), 635 (April) 1943.

<sup>17</sup> Lipschutz, B. Further Contributions to Knowledge of Molluscum Contagiosum, Arch. f. Dermat. u. Syph. **107** 387, 1911.

animal, the routes by which it can be introduced into the animal and the specific immunologic reaction, the last being extremely useful in differentiation of viruses producing apparently identical lesions. The complement fixation reaction proved to be reliable when infected tissues were used as antigen. The best results are obtained by incubation at a low temperature for several hours—the optimal condition for the union of antigen and antibody. Precipitation or flocculation reactions are less reliable. One of the important methods for isolation, cultivation and titration of the viruses and antiviral serums and for study of the local lesions produced by the inoculation was developed in the employment of the chick embryo. Storage of viruses at low temperature gave evidence that they are unstable, become rapidly inactivated at room temperature and can be kept indefinitely and still retain their infectivity. Improvement in methods is largely responsible for the advance in the diagnosis and differentiation of viruses which morphologically are almost identical.

Sulkin and Harford<sup>18</sup> have tabulated the essential items concerned with the laboratory diagnosis of virus diseases in man. In view of the usefulness and accuracy of the table, the section on laboratory diagnosis of the virus infections of the eye is summarized.

1 Herpes. Detection of the virus on the skin and genitalia, neutralization tests, and study of the histopathologic changes and inclusions. The laboratory test of choice is inoculation of the rabbit. Direct inoculation of the chorioallantoic membrane of the developing chick embryo with fluid from a herpetic lesion is a useful procedure.

2 Herpes zoster. Study of the histopathologic changes and inclusion bodies and biopsy.

3 Trachoma and inclusion conjunctivitis. Detection of virus in the conjunctiva and in the genitalia in the latter disorder as well, histopathologic examination and study of the inclusions, and smears. In the diagnosis of trachoma the monkey is the animal of choice for transmission of the disease.

4 Epidemic keratoconjunctivitis. Detection of the virus in the conjunctiva, the neutralizing test, histopathologic examination and inoculation of the mouse.

5 Verruca vulgaris and molluscum contagiosum. Histopathologic examination, study of the inclusions and biopsy.

18 Sulkin, S. E., and Harford, C. G. The Laboratory Diagnosis of Virus Diseases, *J. A. M. A.* **122** 643 (July 3) 1943.

#### EPIDEMIC KERATOCONJUNCTIVITIS

The first epidemic of keratoconjunctivitis recorded in the literature appeared in 1889 in Vienna (Weiss<sup>19</sup> erroneously gave the date as 1893) and was reported by Adler,<sup>20</sup> von Reuss<sup>21</sup> and Fuchs<sup>22</sup> in the same year and by von Stellwag in 1890.<sup>23</sup> The observations, descriptions and morphologic designations of the first epidemic by these four authors showed discrepancies and, accordingly, led to different designations of the disease. Fuchs described the disease as *keratitis punctata superficialis*, Adler, as *keratitis subepithelialis*, von Reuss, as *keratitis maculosa*, and von Stellwag, as *keratitis nummularis*.

In his paper, Fuchs<sup>22a</sup> reported his experience in the observation of 36 cases, he described the disease as *keratitis punctata superficialis* in the first edition of his textbook<sup>22b</sup> and therefore felt he should retain the same term in his paper. With classic clarity, he noted the clinical propensities and the possible etiologic classification of the disease. According to Fuchs, the corneal lesion is similar to herpes febrilis corneae, without formation of vesicles. The onset is characterized by severe acute conjunctivitis, accompanied by pronounced ciliary congestion, there is no secretion or pus, but pronounced lacrimation, pain and photophobia are present. In a few days or weeks the corneal changes follow in the form of small gray spots, usually numbering ten to twenty, but often reaching one hundred. The foci are scattered over the entire cornea or are massed in the central portion. The individual spots are sharply outlined and consist of minute dots, they are located in the superficial layers of the stroma, the epithelial layer bulging over the infiltrates. When the epithelium is lifted off, the infiltrates in the superficial layers are exposed. The irritation disappears within a short time, on the other hand, the spots persist for many months. The centrally located infiltrates result in visual impairment. In one fourth to one third (more than 30) of Fuchs's cases the condition occurred simultaneously in the two eyes and was equally distributed. The disease

19 Weiss, C. Bacteriologic Observations on Infection of the Eye, *Arch. Ophth.* **30** 110 (July) 1943.

20 Adler, H. Keratitis Subepithelialis, *Centralbl. f. prakt. Augenh.* **13** 289, 1889.

21 von Reuss, A. Keratitis Maculosa, *Wien klin. Wchnschr.* **2** 665, 1889.

22 Fuchs, E. (a) *Keratitis Punctata Superficialis*, *Wien klin. Wchnschr.* **2** 37, 1889, (b) *Lehrbuch der Augenheilkunde*, Leipzig, F. Deuticke, 1889.

23 von Stellwag, C. A Peculiar Form of Corneal Inflammation, *Wien klin. Wchnschr.* **2** 613, 1889, **3** 660, 1890.

was often preceded by catarrhal symptoms of the respiratory tract, rarely by herpes of the face. The superficial location of the foci, in conjunction with involvement of the respiratory tract, showed a similarity to herpes. But the absence of a herpetic eruption on the face, the bilateral distribution, the short duration of the acute inflammatory symptoms and, furthermore the large number of infiltrates constantly present differentiated the condition from herpes. Vesicles, epithelial defects and ulceration did not occur. Involvement of the deeper parts, such as iritis or hypopyon, was not observed. The condition lasted many months, and exacerbations were frequently noted. In 14 of the 18 cases cited in his textbook<sup>22b</sup> the disease persisted for from six months to a year. Only after the lapse of one or two years could one be assured of the complete disappearance of the corneal foci. Prolonged observation of the patients compelled Fuchs to change the opinion stated in his textbook, namely, that ulceration occurs but rarely (in 4 cases). The age of one-half the patients varied from 10 to 20 years, the others being rarely less than 10 years old and frequently 40 or older. Most of the cases occurred in the coldest period of the year, between December and March.

The same epidemic was described by the three other authors. Adler's<sup>20</sup> description of keratitis subepithelialis centralis agreed with that of Fuchs. Von Reuss<sup>21</sup> noted somewhat larger infiltrates which were peripherally situated in the cornea. Most of the differences existed in von Stellwag's<sup>23</sup> observations, in which the infiltrates appeared coin shaped, measured 1.5 mm and often showed epithelial defect and ulceration. The infiltrates were not only in the superficial layer of the cornea but in various layers of the stroma, the area of predilection was the periphery, not the center, of the cornea. Iritis was often noted. Healing was rapid, in two to fourteen days, in contrast to the extremely protracted period before clearing up of the lesions reported by the other authors. The differences in the clinical appearance and the duration of the disease led Fuchs to suggest that von Stellwag might have studied a different condition, despite the fact that the disease also was usually bilateral in his cases.

After an interval of eleven years, the disease appeared in Bombay, between January and April of 1901, and disappeared with the approach of hot weather. Herbert<sup>24</sup> observed 226 cases, in which the usual duration was from two to three weeks and the attack was almost invariably

limited to one eye. Only in a case of subacute trachoma were both eyes typically involved. In another case in the epidemic the second eye was mildly affected while the first was recovering. There were no symptoms of nasal catarrh. Most of the patients were young adults, those in the 20 to 30 year age group being most commonly affected.

Clinically, the lesion consisted of minute spots, scarcely at all opaque and easily escaping detection until stained with fluorescein. The corneal surface appeared rough, with slight elevation of the epithelium. As the period of healing approached, the eruption tended to be confined to the central part of the cornea. Thickening of the limbus and moderate conjunctival and ciliary congestion formed part of the clinical picture, the latter being of variable degree and often absent.

The disease approached the proportions of a real epidemic in Madras, India, in 1920, 1928 and 1930. The published report was made by Kirkpatrick,<sup>25</sup> who described a greater incidence in males than in females, the disease being most frequent in persons between 25 and 45 years of age (the number was not given). There was absence of local reaction and evidence of general disease or constitutional defect, lacrimation and photophobia were occasionally noted, and the disease was unocular. Three clinical types were noted. In the first, or superficial, type infiltrates, pinpoint to pinhead in size, irregularly dotted the corneal surface. The disturbance affected chiefly the pupillary area, irritation was noted only when the infiltration was in close approximation to the limbus. A vascular reaction, either circumcorneal or conjunctival, was not noticeable. In the second type the punctate character was lost. One large patch nearly always had a denser portion, which was often linear and somewhat raised. The soft opacity of the large patch faded away into the normal cornea. The patch involved a quadrant of the cornea. This lesion, with possibly a few smaller spots at some distance from it, represented the most common form. The third type was the single, dense, sharply circumscribed spot, with slight elevation and some vascularization when the lesion was situated especially close to the limbus. Irritation was more severe, and the tendency to clear up was less evident in this type than in the first and second types. The duration of the disease varied with the type, the punctate form clearing up in two or three weeks and the last form persisting a year or longer. The epidemic was

<sup>24</sup> Herbert, H. Superficial Punctate Keratitis, *Ophth Rev* 20 339, 1901

<sup>25</sup> Kirkpatrick, H. An Epidemic of Macular Keratitis, *Brit J Ophth* 4 16, 1920



not characterized by the frequent accompaniment of corneal herpes

In his first paper Wright<sup>26</sup> reported 923 cases (1928-1929). The epidemic increased in intensity in the second half of 1929, and by the end of the year he had observed 3,500 cases. By February 1930 the epidemic had practically disappeared. Of the first 923 cases, the disease was unilateral in all but 6 cases, in which it was bilateral. In 2 of these 6 cases the two eyes were attacked at the same time. The duration of the corneal opacities varied from one week to more than a year. In the first series there were 772 males (the incidence being highest between the ages of 20 to 30) and 151 females. In 88 of 225 cases tests with fluorescein gave negative results. Wright emphasized the acute onset, with involvement of the cornea and conjunctiva and the usual occurrence in one eye only. The discrete opacities were localized in the superficial layers of the cornea, they varied in size and number from a multitude of fine gray points, visible only with the loupe, to isolated dots discernible with the naked eye. The epithelium was smooth but might be raised, actual vesiculation was uncommon. The onset was similar to that of mild conjunctivitis and was possibly associated with, or followed by, catarrhal involvement of the respiratory tract. Vision was rarely interfered with to any great extent. There was no iritis, but hypotonia was often present. The relation of superficial punctate keratitis to keratitis disciformis and herpes febrilis corneae produced a different disease picture in each case.

In the first series of cases the external signs were mild, the onset was similar to that of slight catarrhal conjunctivitis or hyperemia, edema of the lid with chemosis suggesting acute inferior conjunctivitis. Photophobia and lacrimation were present. There was almost complete absence of conjunctival discharge. Discomfort was negligible. In the second series the external signs were more pronounced, the eyes having an intensely red appearance, due to increased virulence of the organisms through frequent passage.

The corneal opacities varied from delicate dots, detectable only by the slit lamp, to large solitary, disciform infiltrates. The interval between the appearance of the conjunctival hyperemia and that of the corneal lesions was usually six days, but longer intervals occurred. In some cases the corneal dots showed elevation of the surface and enormous variation in number. In a large majority of cases the infiltrates disappeared in

two months, in other cases they persisted as faint, rounded macular spots (occasionally annular), in rare instances resulting in dense white cicatricial tissue. The corneal sensibility proved to be normal, even in the most severe forms of the disease. The commonest lesion consisted of the small gray dots, often at first only one or two dots appeared, close to the engorged and edematous limbus, and in the next day or two the entire cornea might be involved. The enormous variation in the size and number of the lesions, also, was an integral part of this epidemic, the number ranging from one to a hundred. The foci were peripheral or confined to the pupillary area and were quadrantal in form. The lesions appeared in fine curdlike flakes, with ill defined outlines in the epithelium and probable extension into Bowman's membrane. Their elevation frequently produced eminences in the zone of specular reflection. A second type of opacity was angular, sharply defined, densely opaque, usually round and visible with the naked eye. The lesions varied from minute points to large areas measuring 2 mm in diameter. Large disks developed from smaller ones. Lesions representing transitions from the annular to the disciform type, of 3 mm diameter, were seen, the latter involving the entire thickness of the cornea, with hazy outlines and pronounced corneal swelling. The lesion of the superficial layers was accompanied even in the mildest form, by fine deposits of the endothelium and possible folding of Descemet's membrane, with large pigmented deposits, the deposits in rare instances being larger than the superficial opacities.

The bilateral appearance of the disease was more frequent in the second series of cases, occurring in 16 of the last 1,000 cases, as compared with 6 of the first 923 cases. The second series differed, furthermore, in the presence of tenderness of the preauricular glands, which was first noted at the end of the epidemic in 2 cases of a severe form. Once attention was called to the presence of this tenderness, it was found to be part of the clinical picture in 6 cases of less severe form. This feature may have been unnoticed in the earlier cases, but was undoubtedly absent in many cases in which the disease was of average severity.

Viswalingam,<sup>27</sup> in Malaya, observed only 2 cases of the disease in 1934, but between 1925 and 1938 the epidemic produced 3,521 cases (2,366 of males and 1,155 of females). He identified the epidemic with that of macular kera-

26 Wright, R. E. Superficial Punctate Keratitis, *Brit J Ophth* 14 257, 1930

27 Viswalingam, A. Epidemic Superficial Keratitis in Malaya, *Brit J Ophth* 25 313, 1941

titis reported by Kirkpatrick, a disease already acknowledged by Wright to be identical with the condition which he described as superficial punctate keratitis and with the disease in the epidemic of 1931-1932 in Bengal, observed by Kirwan<sup>28</sup>. Again, the onset was sudden and unilateral, with possible involvement of the second eye one or two days later. Next to the photophobia and lachrimation, swelling of the lids, especially of the outer third of the upper one, dominated the picture. The swelling gave a baggy appearance in the severe forms, like that in lymphostasis, reminding one of a wasp sting. The palpebral and bulbar conjunctivas between the cornea and the outer canthus were severely inflamed, with subsequent chemosis, which often spread over the entire bulbar conjunctiva. In the great majority of cases hardly any mucoid or purulent discharge was present, but invariably the preauricular gland was swollen, and occasionally the submaxillary gland, and in rare cases even the cervical glands, were enlarged. The infiltrates were punctate and superficial, in some cases uniformly studding the entire cornea and in others being scattered. The spots were grayish and occasionally coalescent, erosion and elevation of the epithelium occurred in rare instances. In some cases the superficial infiltration extended to the deeper layers of the stroma, to Descemet's membrane or even to the uvea. The duration of the lesions was stated to be several weeks, but in some cases the spots persisted for two years. Vesiculation, or blisters, not infrequent in Kirwan's series, were consistently absent. The frequency of involvement of the preauricular gland was more characteristic in this series than in Wright's.

In Tasmania, Hamilton<sup>29</sup> managed an epidemic of 92 cases of keratoconjunctivitis between July 1932 and November 1934, before and after this period only endemic cases were observed. Forty-two males and 50 females were affected; the incidence was highest in males in the third decade of life and in females in the fifth and sixth decades. In 25 of the 92 cases the disease was bilateral, in 6 cases the eyes were simultaneously involved, and in another 9 cases the average interval between the appearance of involvement of the two eyes was seventy-eight days, the minimum period being two days and the maximum eighteen months. In 16 cases a

relapse occurred in the affected eye after an interval ranging from three days to four years. In 3 cases the superficial punctate keratitis led to multiple corneal erosions, in 17 cases, to marginal keratitis with and without ulceration, in 3 cases, to dendritic ulcer, and 1 case, to disciform keratitis. The last complication was observed concurrently with superficial punctate keratitis by other authors, such as Wright and Grueter.

Doggart's<sup>30</sup> study included 43 cases, the disease being unilateral and not associated with any other illness, except in 4 cases. The time required for absorption of the dots was stated to be from a fortnight to many months.

The morphologic concept of superficial punctate keratitis, defined as a definite condition by Fuchs, is applicable to any pathologic lesion consisting of opaque dots which involve the epithelial layer, Bowman's membrane and the superficial layers of the stroma. The reason that this group of lesions forms a definite disease entity is evident when the epidemic proportions, the sudden widespread appearance in different localities after the lapse of many years and the etiologic factors in the epidemic are considered.

The epidemic in Calcutta from July to September 1932 consisted of 175 cases. Sanyal<sup>31</sup> described the disease as usually unocular and as affecting males more often than females. The onset was characterized by coryza, without elevation of temperature or glandular involvement. Recovery usually occurred within a week or ten days, in 8 per cent of the cases three weeks was required, and in only 1 case did one month elapse before complete disappearance of the symptoms. The corneal lesions were of four forms: (1) the punctate type, most dense in the central portion and fading toward the periphery, (2) the linear type, with the diameter of a hair, consisting usually of one (most common) or two wavy lines, with tapering ends and no branching, the lines crossing each other when double, (3) a combination of the two varieties, and (4) loss of corneal luster, extending from the limbus to the center, or a band of homogeneous opacity completely encircling the periphery of the cornea in somewhat annular fashion. The corneal sensitivity was normal.

During World War I no epidemic of keratoconjunctivitis broke out, but during the present conflagration epidemics of large proportions have

28 Kirwan, E. W. Epidemic Superficial Punctate Keratitis in Bengal, *Folia ophth orient* **1** 345, 1934.

29 Hamilton, B. J. Survey of Superficial Punctate Keratitis in Tasmania, with Survey of a Mild Epidemic, *Brit J Ophth* **25** 1, 1941.

30 Doggart, J. H. Superficial Punctate Keratitis, *Brit J Ophth* **17** 65, 1933.

31 Sanyal, S. Epidemic Superficial Keratitis, *Am J Ophth* **16** 390, 1933.



been observed in Germany and in the United States

From March to October 1938, zur Nedden<sup>32</sup> observed 127 cases of superficial punctate keratitis. The condition was characterized by an incubation period of eight days and a long duration extending as a rule to three months. In a second report on observations through a continued period, up to February 1939, the number of cases was stated to rise to 200, and in a third paper the number was reported to be 500. In the majority of cases the occurrence was spontaneous, but in 35 per cent superficial injuries preceded the disease. Chemosis of the conjunctiva, swelling of the lids and the preauricular gland, follicular conjunctivitis and subconjunctival hemorrhages were associated with punctate superficial lesions of the cornea. Involvement of the conjunctiva was usually bilateral, the cornea was rarely involved. Males between 20 and 50 years of age were chiefly affected, children below 12 were free from the disease. Sensibility of the cornea was normal, the epithelial cover of the lesions was loose and easily removable with forceps. The punctate changes were of long standing, the dots being visible even after nine months, and the coin-shaped lesions outlasted even the punctate foci. In 1 case there was a duration of two years. In 5 cases keratitis filiformis was noted. According to zur Nedden, no relation exists between superficial punctate keratitis and herpes.

Smitmans<sup>33</sup> reported about 150 cases of epidemic keratoconjunctivitis, in which the onset began with catarrhal symptoms of the nose and throat, or in rare instances with griplike symptoms, accompanied by fever. The disease was characterized by swelling and inflammation of the conjunctiva, chemosis, petechial hemorrhages, seromucous, nonpurulent secretion, and swelling of the lymph glands. The corneal infiltration was intraepithelial in the central portion but extended into the superficial layers of the stroma at the periphery. In the early stages the infiltrates stained with fluorescein. The corneas of both eyes were usually involved, in some cases to a very slight degree, as revealed by examination with a slit lamp. Vascularization and iritis were not observed. The period of incubation was five to ten days.

Ohm<sup>34</sup> observed 700 cases without conjunctival hemorrhages, the absence of which is also characteristic of conjunctivitis due to pneumococci. Swelling of the preauricular glands, with a slight rise in temperature, was often noted. Involvement, even in the severe forms, was frequently unilateral. In about 50 per cent of cases corneal complications were present in varying degrees of severity after the clearing up of the conjunctival changes. The infiltrates, measuring 2 to 3 mm, were usually centrally located and extended below Bowman's membrane; they showed improvement only at the end of six to eight weeks. Dendritic keratitis did not appear in this series of cases, but herpetic vesicles, covering the entire cornea, were of common occurrence, especially toward the end of the epidemic.

Senger<sup>35</sup> first reported about 500 cases, and later another series of about 500 cases. Corneal complications occurred in 30 to 40 per cent of the cases, as a secondary infection, the epithelial layer being involved. The disease was usually unilateral, with chemosis of the conjunctiva, edema of the lids, subconjunctival and subcutaneous hemorrhages and swelling of the preauricular gland. Like Senger, Goedbloed<sup>36</sup> described the clinical manifestations of the epidemic as characteristic of superficial punctate keratitis, with catarrhal rhinitis but without swelling of the preauricular gland. Possibly the nose is the portal of entry, but primary infection of the eye is not excluded in some cases. Schwitalla<sup>37</sup> reported 129 cases with typical onset, unilateral involvement, conjunctival hemorrhages, swelling of the preauricular gland and diminished sensitivity of the cornea. Ulceration was not observed. Males were chiefly affected. Of 129 cases, the condition was unilateral in 106 cases and bilateral in 23 cases.

In the German epidemic different designations were used—keratitis superficialis epidemica (Schultze<sup>38</sup>), keratoconjunctivitis epidemica (Schneider<sup>39</sup>), keratoconjunctivitis of 1938

34 Ohm, W, in discussion on Smitmans<sup>33</sup>

35 Senger, W. Conjunctival Disease of Unknown Origin, *München med Wchnschr* **85** 1810, 1938, **86** 607, 1939

36 Goedbloed, J. Keratoconjunctivitis Punctata Superficialis, *Ophthalmologica* **99** 436, 1940

37 Schwitalla, H. Epidemic of Keratoconjunctivitis Nummularis (Dimmer), *Klin Monatsbl f Augenh* **102** 491, 1939

38 Schultze. Keratitis Superficialis Epidemica, *Klin Monatsbl f Augenh* **102** 425, 1939

39 Schneider, R. Epidemic of Keratoconjunctivitis in Munich and Surroundings, *München med Wchnschr* **85** 1981, 1938

32 zur Nedden, M. Epidemic of Keratitis Superficialis, *Klin Monatsbl f Augenh* **101** 567, 1939, Keratitis Superficialis, *ibid* **102** 487, 1939, Observations on Five Hundred Cases of Epidemic Keratoconjunctivitis, *ibid* **105** 424, 1940

33 Smitmans, F. K. Symposium on Epidemic Keratoconjunctivitis, *Med Klin* **35** 235, 1939

(Smitmans<sup>33</sup>), superficial punctate keratitis (zur Nedden<sup>32</sup>, and Bartels and Loens<sup>40</sup>), epidemic herpetic keratitis (Becker<sup>41</sup>) and keratoconjunctivitis nummularis Dimmer<sup>42</sup> (Meissner,<sup>43</sup> Ješe,<sup>44</sup> Schwitalla<sup>37</sup>) Most of the observers in the English literature and part of the German authors, although using different designations, accepted Fuchs's classification of superficial punctate keratitis The group following Dimmer, however, classified the disease clinically as nummular keratitis

Dimmer<sup>42</sup> reported 4 cases of corneal disturbance, he described the lesions as corresponding closely to those originally described by von Stellwag but as differing notably in having a duration of many months, in contrast to the rapid healing within ten to twelve days in von Stellwag's cases Salzmann<sup>45</sup> collected 88 cases of the disease, the lesions being unilateral in 86 cases and present simultaneously in the two eyes in 1 case In 1 case an interval of four years preceded the involvement of the second eye In Salzmann's opinion, superficial punctate keratitis and nummular keratitis differ only quantitatively, multiplicity of foci and formation of facets being characteristic of both In superficial punctate keratitis there is slight conjunctivitis, without secretion but with pronounced ciliary congestion From the start the disease represents a keratitis, the congestion of the conjunctiva being only symptomatic In the nummular variety of keratitis the individual foci are large, with a diameter of 2 or 3 mm, but even larger ones are not exceptional, especially lesions with irregular outlines In the later stage the surface is depressed, but the failure to stain with fluorescein indicates that the epithelial covering is intact The formation of facets is explained by the location of the infiltrate below Bowman's membrane, so that

a slight depression of the membrane occurs in the stage of resorption The presence of facets on the corneal surface belongs not only to the picture of nummular keratitis but to that of superficial punctate keratitis, contrary to the observation of other authors (Aust<sup>46</sup>)

Aust<sup>46</sup> based his opinion on 27 cases of keratitis nummularis, occurring within seven years, the period coinciding with that of Salzmann's<sup>45</sup> observations The majority of the patients (20 of 27) were farmers Almost without exception, the involvement was unilateral (Dimmer and Aust each noted 1 case of bilateral involvement) and was not associated with irritation of the eyes, the conjunctiva was almost normal, even when the disease was bilateral, the two eyes were not attacked simultaneously The foci usually numbered ten, and often twenty, in 1 case twenty-two foci, usually occupying the central portion of the eye, were noted Depending on the stage of development, the dots were of three types, with numerous transitional forms (1) the superficial small dots, 0.5 mm in diameter, (2) the coin-shaped dots, from 1 to 1.5 mm in diameter, and of long standing, which were somewhat deeper and were associated with swelling of the cornea, folding of Descemet's membrane, slight cloudiness of the aqueous and almost imperceptible irritation of the iris, and (3) formation of facets Depression of the corneal surface was present even years later, the formation of facets being as characteristic as the multiplicity of the foci Sections revealed a normal Bowman membrane, with thinned-out stroma Aust noted the presence of facets one year, and Salzmann even ten years, after the acute stage of the disease Vascularization occurred in 2 of Dimmer's<sup>42</sup> 4 cases There was no recurrence, but healing was extremely protracted, four to five months might elapse before the formation of facets began Aust disagreed with Salzmann in that he denied that the nummular type was identical with the superficial punctate type of keratitis Only the multiplicity of dots is common to the two diseases The superficial punctate variety may exhibit as many as a hundred dots, which necessarily are extremely small, even smaller than the usual dots, of 0.5 mm diameter Furthermore, the dots disappear completely, without formation of facets The nummular variety rather resembles disciform keratitis, the disk-shaped configuration, the absence of ulceration, the location in the upper layers of the stroma and,

40 Bartels, M, and Loens, M Causative Agent of Epidemic Keratoconjunctivitis, *Klin Monatsbl f Augenh* **106** 83, 1941

41 Becker Epidemic Herpetic Inflammation of the Eyes, *Klin Monatsbl f Augenh* **102** 866, 1939

42 Dimmer, F Nummular Keratitis and Related Inflammation of the Cornea, *Ztschr f Augenh* **13** 621, 1905

43 Meissner, W Epidemic of Nummular Keratitis (Dimmer) in Bavaria, *Munchen med Wchnschr* **85** 1939, 1938, Nature of Epidemic Occurring in Germany in 1938-1939, *Deutsche med Wchnschr* **66** 517, 1940

44 Ješe, L Nummular Keratitis, *Klin Monatsbl f Augenh* **96** 219 1936, **100** 874, 1938, Keratitis Nummularis Epidemica, *ibid* **103** 97, 1939

45 Salzmann, M Keratitis Associated with Herpes, *Verhandl d ophth Gesellsch* **42** 303, 1928, Keratitis Nummularis (Dimmer), *Arch f Ophth* **132** 399, 1934

46 Aust, O Keratitis Nummularis, Dimmer, *Arch f Ophth* **129** 576, 1933, Epidemic Nummular Keratitis, *Ztschr f Augenh* **82** 167, 1933

finally, the long duration, without any irritative symptoms, being characteristic of both types. The disciform variety, with its large long centrally located patch, differs from the nummular form, with its multiple and smaller foci. Furthermore, the concentric arrangement is usually missing in nummular keratitis. The disciform variety never shows facets but is known to recur, on the other hand, the nummular type does not show recidivation. In spite of some resemblance to keratitis disciformis, the nummular form represents a distinct condition. With regard to the etiologic aspect, Aust, again, differed from Salzmann, the latter stating that the disease was of possible herpetic origin, while the former assigned it a mycotic origin. The occurrence of the disorder in the summer months (from August to September) probably gives additional support to the mycotic theory. In the subsequent discussion on Aust's paper, Lindner expressed the opinion that the disease is possibly mycotic, and A. Fuchs compared it to "rice mud" keratitis, seen in the Netherlands East Indies and in Ceylon. On the other hand, on the basis of his experience in 25 observed cases, in 1 of which the disease was bilateral, Szekely<sup>47</sup> fully accepted Salzmann's opinion. He stated that keratitis nummularis, keratitis vesiculosa and keratitis punctata superficialis are members of the same disease group and are closely associated with keratitis disciformis, in 1 case of keratitis vesiculosa development into keratitis disciformis could be observed. Neame's<sup>48</sup> opinion gave further support to this concept, namely, that superficial punctate keratitis and its grosser forms—nummular and macular keratitis and dendritic ulcers—are different forms of infection with the herpes simplex virus. His observations in a case of dendritic ulcer with two spots of macular or nummular keratitis together with herpes of the mouth and lids, and in another case of superficial punctate keratitis and two small dendritic ulcers with facial herpes speak not for a coincident but for an identical origin.

Meissner's<sup>43</sup> observations during the epidemic of keratoconjunctivitis in Germany led him to the conclusion that the disease belonged to the keratitis nummularis type (Dimmer). The conjunctival changes were atypical, and the diagnosis was certain only when the cornea became involved. Ulcerations did not occur, but recurrence was not uncommon. The corneal sensitivity

diminished, as in herpes. Jancke<sup>49</sup> agreed with Meissner as to the clinical classification. Ješe<sup>44</sup> reported 77 cases in his first article and 47 in his second article. In 43 of the first 77 cases, the condition occurred in farmers, usually the disease appeared in September. In all but 4 cases the disease was unilateral. The multiplicity of foci was conspicuous, the average number of infiltrates being ten. There were five or less lesions in 16 cases, eleven to fifteen lesions in 10 cases, sixteen to twenty lesions in 4 cases, twenty-one to twenty-five lesions in 5 cases, twenty-six to thirty lesions in 2 cases and thirty-two lesions in 1 case. Clinically, the lesions presented the picture outlined by Salzmann<sup>45</sup> and Aust<sup>46</sup>, round infiltrates of densely packed dots, which were gray and later yellowish, and were of unequal size and arranged in groups, of superficial location. The foci had a long duration and terminated in formation of facets. Contrary to the opinion expressed by Aust, vascularization was frequent. The same feature was mentioned by Dimmer<sup>42</sup> and was noted frequently by Salzmann, especially in cases in which the infiltrates were close to the limbus. Deposits developed in 4 of the cases and iritis in 1 case and confluent patches often caused folding of Descemet's membrane. Ješe<sup>44</sup> theorized on the possibility that the disorder belonged to the herpes group, as postulated by Salzmann, who observed the transition of the nummular into the dendritic type and of the dendritic into the disciform type. His concept was further supported by his observation of the simultaneous presence of herpes simplex corneae in 2 instances. In 1 of these, a case of recurring herpes, the transition to keratitis nummularis was demonstrated. Contrary to the opinion expressed by Aust, Salzmann's assumption that the onset consists in the appearance of multiple lesions within the cornea has been corroborated. Reichling's observation of keratoconjunctivitis epidemica in one eye and dendritic keratitis in the other is further evidence in support of a herpetic origin. Becker<sup>41</sup> compared the disease in his cases to the keratitis epithelialis vesiculosa disseminata described by Vogt, which was characterized by two to ten epithelial vesicles or defects, often accompanied by herpes of the lips. In Sacha's<sup>50</sup> 2 cases,

49 Jancke, G. Mechanism of Development of Nummular Keratoconjunctivitis Epidemica, *Klin Monatsbl f Augenh* **105** 7, 1940, Identity of Keratoconjunctivitis Nummularis Epidemica and Diseases Described from 1889 to 1941 Under Various Names (Keratitis Punctata, Nummularis, Maculosa, Epidemica, etc.), *ibid* **108** 39, 1942.

50 Sacha, A. Keratitis Nummularis (Dimmer), *Arch f Ophth* **131** 102, 1933.

47 Szekely, J. Keratitis Nummularis (Dimmer), *Arch f Ophth* **134** 184, 1935.

48 Neame, H. The Association of Dendritic Ulcer of the Cornea and of Superficial Punctate Keratitis with Herpes Facialis, *Brit. J Ophth* **21** 298, 1937.

those of a 5 year old girl and a man aged 22, the disease was of the same type, the diagnosis being based on quantitative, rather than on qualitative, differences the second case having features similar to those of disciform keratitis

Scheerer<sup>51</sup> emphasized the stubborn resistance to treatment and the frequent recurrence. His cases were characterized by mild conjunctival symptoms, with corneal complications occasionally at the onset, the corneal lesions staining with fluorescein. The changes in the cornea were protean and involved the epithelial, subepithelial and superficial layers as dustlike delicate pointlike or larger spots. They were scattered as irregular projections over the entire cornea, with a predilection for the center. Sometimes delicate folding of Descemet's membrane and slight hyperemia of the iris were observed, as well as plastic iritis, in 1 case. Opacities in the vitreous and episcleritis, frequently with a swollen preauricular gland, were also noted. The early stages were similar to those of superficial punctate keratitis, the late stages resembled the nummular type.

Meesmann and Bachmann<sup>52</sup> reported 250 cases in which there were swelling and redness of the caruncula, and later the semilunar fold, and often ptosis. Follicles were present on the inflamed upper fornix, swelling of the preauricular gland was noted in severe forms of the disease. The severity of the corneal complications was inversely related to that of the conjunctival symptoms. The severe form of conjunctivitis healed within three or four weeks without any corneal involvement. In 15 per cent of cases the cornea was involved, with a duration of four to five months. Healing did not produce immunity, in a case of unilateral, severe conjunctivitis lasting three months, the second eye became affected after an interval. The sensitivity of the cornea was diminished. The corneal lesions appeared first in the center and later in the periphery. They extended from the superficial into the deeper layers, and healing left a mild depression of the surface, as a result of absorption, with subsequent irregular astigmatism. Wolter<sup>53</sup> expressed the belief that epidemic keratoconjunctivitis was nummular in form, iritis and cloudi-

ness of the aqueous, with swelling of the lymph glands, being present only in exceptional cases.

The first observation of American authors on the epidemic was made by Merrill,<sup>54</sup> who described clinical manifestations similar to those outlined by Wright. Several members of the same family had the disease, the duration of which was from three to eighteen months, in some cases even longer. Swelling of the preauricular gland was observed only in rare instances. Hobson<sup>55</sup> reported about 16 cases, in which the onset was marked by violent conjunctivitis (unilateral only in 1 case). The bulbar and the palpebral conjunctiva were equally red and swollen in the two eyes. In contrast to the similar involvement of the conjunctivas of the two eyes, the cornea of one eye was more severely affected than that of the other eye. The number of stainable dots varied from twenty to one hundred, they were minute and grayish and were situated in the second layer of the cornea. One patient had a corneal ulcer, with the triangular base down. The peculiar arrangement of the deposits may be explained by their mode of origin. Hobson stated

They are conglomerations of cells held in masses by fibrin. Motion of the eyeball and gravity may have played a part in placing them in this position. With the aid of a slitlamp it was possible to make out very minute deposits forming a faint haze on the basal layers of the corneal epithelium. In our more severe cases, the cornea appeared rough and uneven.

Thygeson<sup>56</sup> observed that follicular hypertrophy of the conjunctiva was more pronounced in the lower fornix, in association with an enlarged preauricular gland and scanty secretion, composed of mononuclear elements. Complete resolution required from one to three weeks. Bacteriologic examination gave negative results. The lesions appearing in a minor epidemic in Iowa in 1935 resembled the follicular type of inclusion conjunctivitis but differed in the predominance of mononuclear elements (in contrast to the presence of neutrophilic leukocytes in the acute stage of inclusion conjunctivitis), in a shorter duration and in the absence of inclusion bodies. In similar cases observed in New York the lesions were bilateral, with 1 exception. In the latter cases the disease showed acute papillary conjunctivitis, with absence of bacteria and with preauricular adenopathy and scanty secretion, consisting predominantly of mononuclear elements, a picture which led Thyge-

51 Scheerer, R. Epidemic Keratoconjunctivitis, *Klin Monatsbl f Augenh* **105** 110, 1940

52 Meesmann, A, and Bachmann, W. Clinical and Microbiologic Observations in Cases of Epidemic Keratoconjunctivitis, *Klin Monatsbl f Augenh* **105** 1, 1940

53 Wolter, H. Epidemic Ophthalmia (Keratoconjunctivitis Nummularis Epidemica) in Germany, *Klin Monatsbl f Augenh* **107** 113, 1941

54 Merrill, H. G. Epidemic Keratoconjunctivitis Diversiformis, *Am J Ophth* **19** 1007, 1936

55 Hobson, L. C. Acute Epidemic of Keratitis Punctata Superficialis, *Am J Ophth* **21** 1153, 1938

56 Thygeson, P. A Papillary Type of Beal's Conjunctivitis, *Am. J Ophth* **21** 1017, 1938

son to the conclusion that the disease was a papillary form of Beal's conjunctivitis<sup>57</sup>

Hogan and Crawford<sup>58</sup> made an extensive and scholarly study of keratoconjunctivitis epidemica, based on 125 cases. In 31 instances conjunctivitis developed in the second eye after three or four days. When the eyes were involved simultaneously, the condition was more severe with petechial, or even larger, conjunctival hemorrhages. The average duration of the conjunctivitis was stated to be thirteen days. Keratitis developed in 92 cases and was bilateral in 23 cases. Involvement of the cornea appeared two to eight days after the onset of the conjunctivitis. The intense pathologic condition of the conjunctiva was not associated with a discharge. In 7 of Hogan and Crawford's cases a white, fairly thick, extensive pseudomembrane developed, an observation not reported in previous epidemics. The conjunctivitis was of the follicular type in 54 instances. Preauricular, angular, submaxillary or cervical adenopathy was often noted. The sensitivity of the cornea was normal. The corneal changes themselves were classified under three types: (1) the punctate type, in which the lesions stained with fluorescein, were evanescent and healed with regression of the conjunctival involvement, (2) the macular type, characterized by absence of staining, predilection for the center of the cornea, absence of either ulceration or vascularization, folding of Descemet's membrane, in 6 cases, and a tendency to become faint within three months, and (3) the disciform type, with infiltration of 4 mm in diameter. The last form persisted longest and resulted in the poorest visual recovery.

Rieke<sup>59</sup> treated 600 patients with the disease in Portland, Ore., in 1941, the condition being unilateral in most cases. In some instances the second eye became involved, but the symptoms were not as severe as those of the primarily affected eye. Small hemorrhages were of common occurrence. Desquamation of the conjunctiva occurred in ten or twelve days. The duration of the disease averaged from twelve to twenty-eight days, being not less than twelve days in any case. In about 50 per cent of the cases grossly visible dots, 0.5 mm in diameter, appeared on the cornea in large numbers in twelve to fourteen days. Ulceration and vascularization were absent. At the end of two

months there was no change in the pathologic picture of the cornea. Only after seven months was diminution in the size and number of the dots observed.

Berliner<sup>60</sup> reported about 18 cases, in 9 of which the condition was bilateral and in 14 accompanied by corneal opacities. The opacity became less intense only after three months. Sanders and Alexander,<sup>61</sup> Sanders and associates<sup>62</sup> and Sanders, in an address at a meeting of the New York Academy of Medicine, section of ophthalmology, stated the opinion that the condition was a disease entity. The diagnosis was made according to the following criteria, based on observations in 80 cases<sup>62</sup>. The presence of an acute follicular type of conjunctivitis, with occasional pseudomembrane of the conjunctiva of the lower lid, and absence of bacteria. In addition, enlargement of the lymph nodes, scanty discharge, composed of mononuclear cells, and superficial punctate keratitis were almost constant features. In 42 cases the cornea became involved from one week to ten days after the onset of the disease, with no record of absorption at the end of five months. All the patients with severe ocular involvement had systemic symptoms, and in 70 of 80 patients the epidemic keratoconjunctivitis followed ocular trauma or inflammation. In the discussion at the meeting of the Academy, Braley<sup>63</sup> referred to 200 cases of his own, in which the diagnosis was based on 1,600 cases recorded in a survey of the New York state department of health.

Sporadic cases of the disease have appeared all over the world, the first outbreak of epidemic proportions occurring in Vienna in 1889. In the Far East the disease is endemic, there the largest epidemics seem to have occurred in peacetime. As previously mentioned, in the last decade the epidemic became rampant in Germany (Düsseldorf, Munich) and in the United States (on the west and east coasts), where it was more prevalent in cold weather dying out toward spring.

Observers have expressed almost unanimous agreement concerning the absence of bacteria in the epidemic outbreaks, with the exception of Herbert<sup>24</sup>. He described bacilli with a distinct

60 Berliner, M. L. Epidemic Keratoconjunctivitis, *Am J Ophth* **26** 51, 1943.

61 Sanders, M., and Alexander, R. C. Epidemic Keratoconjunctivitis. I. Isolation and Identification of a Filtrable Virus, *J Exper Med* **77** 71, 1943.

62 Sanders, M., Gulliver, F., Forchheimer, L. L. and Alexander, R. C. Epidemic Keratoconjunctivitis, *J A M A* **121** 250 (Jan 23) 1943.

63 Braley, A. E., in discussion on Superficial Punctate Keratitis, Keratoconjunctivitis, *Arch Ophth* **30** 160 (July) 1943.

57 Beal, R. A Specific Type of Acute Follicular Conjunctivitis, *Ann d'ocul* **137** 1, 1907.

58 Hogan, M. J., and Crawford, J. W. Epidemic Keratoconjunctivitis, *Am J Ophth* **25** 1059, 1942.

59 Rieke, F. E. Epidemic Conjunctivitis of Presumed Virus Causation, *J A M A* **119** 942 (July 18) 1942.

capsule and feeble staining qualities, the organism was twice as long as broad and tapered at the ends, which were round, or sometimes slightly curved. Generally the bacilli were single, only rarely were they paired. Experiments in cultivation and inoculation from eye to eye yielded negative results. Axenfeld and Westhoff concurred in Heibert's opinion, but in subsequent epidemics the organism could not be identified. The large number of specimens collected during the epidemic in Bombay were examined by Wight<sup>26</sup> for the presence of bacteria, with negative results. In the widespread epidemics reported by Viswalingam<sup>27</sup> and zur Nedden<sup>32</sup> the results of bacteriologic studies were negative. Smitmans<sup>33</sup> mentioned the presence of mixed bacteria, such as are noted in all cases of acute conjunctivitis, but inoculation of the cornea of the rabbit, as well as intraocular and intracerebral inoculation, gave negative results. Zur Nedden noted diplobacilli and inclusion bodies in the corneal epithelium in 3 of 10 cases in which he made examination, but he refused to attribute any etiologic significance to these observations, especially since some authorities still doubt that these bodies represent living organisms. The inclusion bodies were absent in the cases of his later series. Inoculation of the rabbit cornea did not produce any significant pathologic changes. Meesmann and Bachmann<sup>52</sup> noted a diphtheroid (*Bacillus xerosis*) in symbiosis with staphylococci, Behr<sup>64</sup> and Behr and Zeissler,<sup>65</sup> similarly discovered diphtheroids in their cases. Meesmann and Bachmann concluded that the etiologic role of the micro-organisms of the diphtheroid group was not established, while the latter accepted the diphtheroid as the causal agent, the action of the organisms being weakened as a result of change in virulence. As a logical consequence, diphtheria antitoxin was employed, with good results. Zur Nedden had already taken an energetic stand against Behr and Zeissler's view and ascribed the apparently good results of diphtheria antitoxin to its being a nonspecific therapeutic serum. He noted that children are not subject to epidemic keratoconjunctivitis and, conversely, that they are more susceptible to diphtheria than are adults. Furthermore, from the bacteriologic standpoint, it is worth mentioning that bacilli of the xerosis group are less toxic but may acquire some degree of toxicity in cases of acute conjunctivitis. The possible pitfall in the use of diphtheria antitoxin in treat-

ment of keratoconjunctivitis was pointed out also by Wolter,<sup>53</sup> who called attention to the fact that often the disease disappears spontaneously without any medication or, as in Meissner's case, through the administration of saline solution exclusively. In the epidemic of 1928 Bartels and Loens<sup>40</sup> found *B. xerosis* in the corneal epithelium of patients with superficial punctate keratitis.

The absence of characteristic and constant bacteriologic features did not escape the attention of observers and, consequently, led to another possible explanation of the epidemics, namely, their virus origin. In the earlier years this explanation was necessarily speculative, while in later years, since Grueter's epochal transmission of dendritic keratitis to the cornea of the rabbit, the theoretic suppositions have been replaced by experimental research. These scientific efforts were crowned recently by the success of Sanders and his co-workers in isolating the virus.

The possible herpetic origin, through an attenuated, altered or different virus, had already been suggested by Fuchs, who pointed out that with respect to the location of the infiltrates in the superficial corneal layers and the association with involvement of the respiratory tract, epidemic keratoconjunctivitis resembles herpes but differs from it in the absence of a herpetic eruption on the face, in the absence of vesicles, in the multiplicity of foci, in the more frequent bilateral occurrence and, finally, in a shorter duration. The discovery of the transmissibility of corneal herpes was made by Grueter, in 1918, and after this the occurrence of the major epidemics of keratoconjunctivitis necessarily influenced the search for their causation. Grueter differentiated two forms of herpes virus, the more virulent one being responsible for dendritic keratitis and the less virulent one for the superficial punctate, vesicular and disciform varieties of the disease and for the recurrent corneal erosion. According to Salzmann,<sup>45</sup> the herpes virus is capable of producing various types of lesions, and the superficial punctate type of keratitis is intermediate between the vesicular and the disciform type. Ješe<sup>44</sup> accepted the explanation without any investigation of his own. Zur Nedden<sup>32</sup> denied the existence of any relation between superficial keratitis and herpes and obtained negative results from inoculation of the rabbit cornea. Meissner<sup>43</sup> had similar negative results with the same technique, but both authors, together with Schwitalla,<sup>37</sup> Smitmans<sup>33</sup> and Jancke,<sup>49</sup> accepted the theory of a virus causation. Jancke emphasized that the virus of keratoconjunctivitis cannot be identical with the herpes virus because

64 Behr, C. Keratoconjunctivitis Epidemica, *Deutsche med. Wchnschr.* **66** 515, 1940.

65 Behr, C., and Zeissler, J. Etiology of Epidemic Keratoconjunctivitis, *München med. Wchnschr.* **87** 665 1940.



the former does not show an increase in virulence after animal passage and does not result in general symptoms, not even after intracerebral inoculation. Inoculation of the cornea of rabbits and guinea pigs yielded positive results only in a small percentage of cases, and the disease occurred in milder form than in man. Of 42 corneal inoculations, 14 gave positive results, the lesion consisting of infiltration in the area of the scratch and slight conjunctivitis, with swelling of the lids, dendritic keratitis occurred in only 1 instance. The insertion of pieces of infected human conjunctiva into the conjunctiva of rabbits resulted in the occurrence of various lesions, such as follicular conjunctivitis and punctate and disciform keratitis. Material scratched on the corneas of 15 rabbits produced tongue-like infiltrations radiating from the scratch in 10 animals. Therefore the virus must be related to the herpes virus, or to a similar filtrable virus. The diminished sensitivity of the cornea and the herpetic complications in some cases of punctate keratitis point either to this possibility or to the production of a favorable disposition to herpetic invasion. The petechial hemorrhages of the skin were interpreted by Hamilton<sup>29</sup> as neural lesions due to the virus, and he cited Neame,<sup>48</sup> in whose opinion it was almost certain that one virus, modified perhaps in different localities or in different years, is capable of producing a variety of corneal lesions. Hamilton noted absence of acquired immunity. This is not surprising, since it is known that antibodies are numerous after infection with herpes simplex but do not provide lasting immunity.

With regard to the question of virus causation, Wright observed nuclear and cytoplasmic inclusion bodies suggestive of Negri bodies rather than of the inclusions characteristic of variola. The inclusion bodies were numerous, of varying size and staining quality and in close proximity to the corneal lesion. In 5 of 7 specimens the corneal epithelium stained with hematoxylin and eosin, and patches of minute, ovoid or elongated particles lay on the cells, these particles were not seen in scrapings, could not be cultivated and were thought to be rod organisms. The transfer of an unfiltered suspension of epithelium to the cornea of rabbits produced the disease on the sixth day in 1 of 2 black rabbits and failed to produce the condition in 7 white rabbits. Direct transfer to the cornea gave positive results in 3 of 7 human subjects and negative results in 13 monkeys. Attempts to transfer the disease to the skin of human subjects, as well as to the skin of rabbits and calves, and subdural and intratesticular injections in rabbits

resulted in failure. Filtered material planted on the cornea gave positive results in 5 of 11 human subjects and negative results in white and black rabbits and in monkeys. In conclusion, Wright decided that the agent in the disease must be a specific filtrable virus. Encouraged by these experimental results, Viswalingam<sup>27</sup> instilled conjunctival washings into healthy eyes and produced the disease in 4 of 6 persons, with corneal involvement in 1 of them. The conjunctivitis developed within twelve to thirty-six hours, it was moderately severe and was associated with chemosis and swelling of the preauricular gland. Diesel reported 4 successful "takes" in 8 inoculations of the chorioallantois of chicks, the 9 or 10 day embryos dying in from seventy-two to ninety-six hours after the appearance of edema and opacification of the membrane. In 1 experiment the virus passed through 4 embryos without losing its specificity. Meissner<sup>43</sup> and Goedbloed<sup>36</sup> had negative results in inoculation of the rabbit cornea, and Smitmans<sup>33</sup> had negative results in intracorneal and intracerebral, as well as in corneal, inoculations. Their failure to produce the disease was interpreted as ruling out the possibility that herpes virus was the causative agent, since the rabbit cornea is sensitive to this virus. All these authors and, in addition, Bartels and Loens<sup>40</sup> worked on the assumption that a virus was the causative agent.

The most important experimental work was that of Sanders and Alexander,<sup>61</sup> who succeeded in isolating the virus from the blood of 2 patients. At first, the virus could be sustained by inoculation of tissue cultures with conjunctival scrapings or with emulsified mouse brain. Later, injections of the virus proved fatal to every mouse to which they were given, and the virus could be readily maintained in mice. The virus proved pathogenic for unweaned white Swiss mice when injected intravenously, intraperitoneally and intracerebrally, and for rabbits only when given intracerebrally. The virus passed through E-K Seitz and Berkefeld filters. The mouse virus was not neutralized by anti-lymphocytic-chorion-meningitis serum, antiherpes serum or normal human serum. But neutralization of the virus occurred with serum of the 2 patients from whom the virus was isolated and, furthermore, with the convalescent serum of 3 patients from California and 1 patient from New York who had previously had epidemic keratoconjunctivitis. The mouse virus proved to be slightly pathogenic in a human volunteer, whose serum contained neutralizing antibodies after one month. Antibodies were demonstrated in 7 patients

The isolation of the virus in cases of epidemic keratoconjunctivitis firmly established the disease as a clinical entity, in the same way in which the transmission of dendritic keratitis distinguished the latter from other corneal diseases. The question whether superficial punctate keratitis and nummular keratitis are two varieties of the same disease or are distinct diseases will find a definite answer only in further research. At present opinions differ. Fuchs expressed the belief that the disease picture described by von Stellwag differed so widely with respect to its short duration and the complete recovery of the patient that it might represent a different clinical entity. Dimmer revived the conception of nummular keratitis, Salzmann, Szekely and others stated they would include disciform keratitis in the herpetic group. The isolated occurrence of facial herpes and dendritic or vesicular keratitis with, or preceding, epidemic keratoconjunctivitis seems to support this contention, without furnishing decided evidence. The clinical similarities and dissimilarities previously mentioned neither prove nor disprove the assertion. It is of interest that in the epidemic in Germany some authors seemingly observed clinical manifestations characteristic of superficial punctate keratitis, and others described the disease as nummular keratitis. It has been stated by some observers that when not epidemic the latter form was of mycotic, not virus, origin (Aust, Lindner), that it occurred in farmers and that it terminated in formation of facets. Observations by Ješe, Meissner, Schwitalla, Pillat and Jancke favored the belief that the disease is the nummular type of epidemic keratoconjunctivitis notwithstanding the fact that in the same epidemic superficial punctate keratitis was the predominant form in the observations of zur Nedden and others, as well as in the epidemics of the Far East and of the United States. There are two possible explanations. Either the same virus causes clinically similar, but not identical, lesions, or the epidemic is caused by two different viruses or by a virus and an attenuated form. But the virus of epidemic keratoconjunctivitis differs widely from that of corneal herpes, as proved by Sanders, consequently, there exists a clinical and biologic differentiation, which must be taken into account. The possibility that epidemic keratoconjunctivitis is identical with Béal's conjunctivitis can be eliminated in view of the absence of neutralizing antibodies in cases of Béal's disease, as well as the absence of corneal complications, which is one of the most important features in epidemic keratoconjunctivitis.

## TRACHOMA

Halberstaedter and von Prowazek,<sup>66</sup> in 1907, reported cases in Batavia, Netherland East Indies, in which cellular inclusions occurred in the epithelial cells of the conjunctiva and the disease was transmitted, with identical inclusions, to orang-utans. The minute bodies were first recognized by von Prowazek as the causative agent in trachoma. This cellular inclusion proved to be morphologically identical with that in psittacosis, which, through experiments with collodion membrane filters, was discovered much later to be a filterable virus of comparatively large size. After this discovery an enormous amount of literature appeared showing that the inclusions are most numerous in the superficial epithelium in cases of untreated acute trachoma, are less frequent as the disease progresses and are present in only 50 per cent of cases of long-standing disease. The Giemsa or the Heidenhain iron hematoxylin stain is useful in demonstrating their presence. With the Giemsa stain the inclusions appear light blue, violet or red, and the tiny extracellular granules are uniformly red. Von Prowazek<sup>67</sup> designated the cellular inclusion as a chlamydozoon, to indicate the protistan nature. Confirmatory observations were shortly reported by Stargardt, von Kenedei, Miyajima, Mijaschita, Leber and Greeff, who gave the name trachoma bodies. This term was subsequently changed to elementary bodies, or organisms, by Herzog.<sup>68</sup>

These organisms are now recognized as identical with elementary bodies in other virus diseases. The particles, 0.25 millimicron in diameter, are surrounded by a halo of nonstaining material, frequently exist in pairs and sometimes are connected by a slender filament. The large inclusion bodies are located in the cytoplasm and occasionally in the nucleus. Clumps of elementary bodies are constantly observed in the cell cytoplasm, a small or a large compact mass lying free in the plasma or capping the nucleus. The minute bodies may be so numerous that the entire cytoplasm appears studded with them, or they may be evenly distributed, each being embedded in a pale blue-staining mass of the

66 Halberstaedter, L., and von Prowazek, S. Cellular Inclusions of Parasitic Nature in Trachoma, *Archiv f. Gsndhtsamt* **26** 44, 1907, *Deutsche med. Wchnschr.* **2** 1285, 1907, Significance of Chlamydozoa in Trachoma and Blennorrhoea, *Berl. klin. Wchnschr.* **46** 1110, 1909, **47** 661, 1910.

67 von Prowazek, S. Chlamydozoa, *Archiv f. Protistenk.* **10** 336, 1907.

68 Herzog, H. A New Method of Rapid and Contrast Staining of Trachoma Bodies in Histologic Sections, *Archiv f. Ophth.* **74** 520, 1910.



protoplasm, which Halberstaedter and von Prowazek called plastin-like material. In cases of trachoma and inclusion conjunctivitis initial bodies (Lindner<sup>69</sup>) were described as appearing in the cytoplasm and were stated to be the form from which the elementary bodies develop. They are round and sharply defined and measure 0.6 to 1.0 microns in diameter. According to Lindner initial bodies develop from a ring form and multiply by repeated division to form groups and clusters. In the later stage of development minute, red-staining elementary bodies appear inside the initial bodies. Residual bodies lie inside the cell inclusion (red with the Giemsa stain and blue with the Mallory stain). They are larger than the initial bodies, but as the elementary bodies become more numerous, they diminish correspondingly. In Lindner's opinion they do not represent a phase in the growth of the virus, they are simply nuclear fragments, and not living organisms. The plastin-like mass is considered a degenerative product of the cell in response to the invading virus.

The chlamydozoa of von Prowazek<sup>67</sup> were not easily accepted as the causative agent in trachoma, many authorities explained them as colonies of micrococci, secretion granules or chromatin masses in the cells. Criticism of his theory was based on observations by Gutfreund who noted chlamydozoa only in 47 of 106 cases. Their specificity was also questioned because of their presence in nontrachomatous diseases such as follicular conjunctivitis (Romer), chronic conjunctivitis (Addario), blepharoconjunctivitis (Axenfeld<sup>70</sup>) and conjunctivitis vernalis (Lodato and Thierfelder). Heymann<sup>71</sup> found the chlamydozoa in 4 cases of gonococcal conjunctivitis in the newborn and expressed doubt that they represented living organisms or that they had any connection with the causation of trachoma. In the second article he corrected his previously expressed opinion and stated that these bodies represent a virus pathogenic for monkeys.

Further criticism of the specific nature of these bodies was based on their presence only in the epithelial, and not in the subepithelial layers and in the follicles while trachoma typically involves the deeper layers. Their presence in

sections was interpreted as their being stained granulations of mast cells. The observation of identical inclusions in trachoma and in nongonococcal ophthalmia gave impetus to the revival of Ait's view that the two conditions are different stages of the same disease, and inclusion conjunctivitis was interpreted as trachoma of the newborn, a concept strongly opposed on the basis of the difference in the clinical pictures and the histologic structures of the two conditions. Greeff, the originator of the term trachoma bodies, changed his opinion because of the presence of the inclusions in conjunctival diseases other than trachoma and denied that they had any specificity for trachoma. Led by the same misconception that the morphologically identical inclusions appear only in trachoma and nongonococcal ophthalmoblennorrhoea Herzog,<sup>68</sup> on the basis of cultivation experiments, expressed the opinion that gonococci show forms of involution (microgonococci) and the inclusions represent an aggregation of these forms, an opinion almost universally rejected by other investigators. The results of the cultivation experiments intensified the existing confusion. Schiele reported that he had produced chlamydozoa in pure culture (on ordinary mediums) in 34 cases and transmitted the disease from the culture by inoculation of dogs. Noguchi and Cohen,<sup>72</sup> similarly, reported positive results on culture. Later experience did not confirm these observations. Thygeson and Mengert<sup>73</sup> proved that cultivation was unsuccessful even on the chorioallantoic membrane of the chicken embryo, the classic culture medium of viruses. The question of transmission to animals, however, was settled as it is possible to transmit the disease only to monkeys. The experiments with earthenware filtration usually gave negative, but sometimes contradictory, evidence, and the results could not be considered useful in classification until Thygeson and Proctor<sup>74</sup> proved that the virus passes through collodion membrane filters with an average pore diameter of less than 0.2 micron and therefore is readily filterable. These experimental results were confirmed by Julianelle and Smith<sup>75</sup> and by Stewart. Research on the virus of trachoma, which received a special impetus

69 Lindner, K. The Free Initial Form of Prowazek's Inclusion Bodies, *Wien klin Wchnschr* **22** 1697 and 1742 1909. Staining of Prowazek's Inclusion Bodies, *Zentralbl f Bact* **57** 429, 1910, Biologic Relation Between Inclusion Virus of Trachoma and Bacterium Granulosis Noguchi, *Arch f Ophth* **122** 391 1929.

70 Axenfeld, T. Die Aetiologie des Trachoms, *Jena G Fischer*, 1914.

71 Heymann, B. Sites of the Prowazek Bodies, *Berl klin Wchnschr* **47** 663 1910.

72 Noguchi, H., and Cohen, M. Experiments on the Cultivation of the So-Called Trachoma Bodies, *Arch Ophth* **40** 1, 1911, **43** 117, 1914.

73 Thygeson, P., and Mengert, W. F. The Virus of Inclusion Conjunctivitis, *Arch Ophth* **15** 377 (March) 1936.

74 Thygeson, P., and Proctor, F. I. The Filtrability of Trachoma Virus, *Arch Ophth* **13** 1018 (June) 1935.

75 Julianelle, L. A., and Smith, L. E. Studies on Infectivity of Trachoma, *Am J Ophth* **22** 62, 1940.

from the discovery of similar inclusions in psittacosis, has shown that the inclusion bodies are always present in cases of untreated trachoma. The bodies are filtrable, and the disease can be transmitted to monkeys and apes, but without the formation of pannus or the typical cicatricial involvement which characterizes invasion of the human conjunctiva and the corneal epithelium. According to Perdrau,<sup>76</sup> the possibility exists that all forms of trachoma are not caused by one and the same virus or strains of the virus, and that Egyptian and Brazilian trachoma may represent different strains of the same virus, each possessing fixed characters.

A different group of authors, which included Busacca,<sup>77</sup> Cuenod and Nataf<sup>78</sup> and Poleff, stated that the existing agent in trachoma is a rickettsial organism. Cuenod and Nataf<sup>78</sup> claimed they had successfully recovered rickettsial bodies from the intestine of lice experimentally infected with trachomatous material by the intra-anal route, and had transmitted the disease to a human volunteer by means of crushed lice infected with trachoma. The subject manifested allegedly typical trachoma sixty days after the onset of symptoms. Busacca, who noted inclusion bodies in the epithelial cells and follicles of trachomatous patients, concluded that the bodies were the causative agent and, accordingly, called them the rickettsias of trachoma. This was a premature conclusion, in view of the fact not only that Thygeson<sup>79</sup> was unable to confirm the findings, but that in his opinion, the so-called bodies represent only cell granules and protoplasmic debris. The

rickettsial origin of trachoma was denied by Julianelle and Smith,<sup>75</sup> de Rotth,<sup>80</sup> Braley<sup>81</sup> and Bengston,<sup>82</sup> and the louse cannot be regarded as the vector in trachoma.

*Bacillus granulosis*, described by Noguchi in 1927, was proved not to be the cause of trachoma, but only the etiologic agent in folliculosis of the conjunctiva.

The inclusion bodies of trachoma were observed in two other conjunctival diseases, namely nongonococcal blennorrhea of the newborn and swimming pool conjunctivitis. The inclusion bodies with basophilic cytoplasm had already been discovered by Halberstaedter and von Prowazek<sup>66</sup> in cases of nongonococcal ophthalmoblenorrhea after careful bacteriologic examination had excluded the presence of gonococci. Shortly afterward, Heymann discredited the importance of the discovery by stating that the inclusion bodies are present in gonococcal infection of the conjunctiva, and he consequently explained their presence as a cellular reaction due to the gonococci. Conversely, Staigardt emphasized that the inclusion bodies were present only in the absence of gonococci. Wolfrum and Lindner observed inclusion bodies constantly in nongonococcal conjunctivitis and could not prove their presence in the gonococcal form. These observations, corroborated by other authors, were instrumental in establishing inclusion blennorrhea (inclusion conjunctivitis) as a separate clinical entity, characterized by a milder course than that of gonococcal conjunctivitis, the secretion being much less in amount and rather serous. Furthermore, inclusion conjunctivitis was associated with an almost constant absence of corneal complications and by a longer period of incubation (in adults, seven to ten days, and in the newborn, five to nine days). Lindner succeeded in identifying the inclusion bodies in the urethra and even in the vagina, in cases of urethritis of nongonococcal type. Lindner, Fritsch and Hofstadter produced trachoma-like changes in *Macacus rhesus* monkeys and in baboons through inoculation of the secretion. Morax and Bollack, Nicolle, Cuenod and Blaizot and Botteri and Leber confirmed the transmission of inclusion conjunctivitis to monkeys, even by means of material passed through a Berkefeld filter. The inclusion urethritis of the male and the inclusion cervicitis of the female became recognized as clinical entities in certain countries. But

76 Perdrau, J. R. Virus Infections in Ophthalmology, in Ridley, F. and Sorsby, A. Modern Trends in Ophthalmology, New York, Paul B. Hoeber, Inc., 1940, p. 32.

77 Busacca, A. Frequency of Corneal Complications in Trachoma, *Rev. internat. du trachome* **10**: 57, 1933, Structure of Herbert's Pits, *Compt. rend. Soc. de biol.* **117**: 715, 1934, *Brit. J. Ophth.* **19**: 26, 1935, Anatomicopathologic and Clinical Observations on Pannus Trachomatousus of the Cornea, *Arch. Ophth.* **11**: 730 (April) 1934, Is Trachoma Rickettsial Disease? *ibid.* **17**: 117 (Jan.) 1937.

78 Cuenod, A., and Nataf, R. Le trachome, Paris, Masson & Cie, 1930, Contagiosity of Trachoma, *Arch. d'opht.* **50**: 261, 1933, Possible Role of Rickettsia in Causation of Trachoma, *ibid.* **53**: 355, 1936, Bacteriological and Experimental Researches on Aetiology of Trachoma, *Brit. J. Ophth.* **21**: 309, 1937, Experimental Trachoma, *Ann. d'ocul.* **174**: 433, 1937, Etiology and Pathogenesis of Trachoma, *Rev. internat. du trachome* **14**: 117, 1937.

79 Thygeson, P. Microbic Etiology of Trachoma, *Arch. Ophth.* **11**: 728 (April) 1934, Nature of Elementary and Initial Bodies of Trachoma, *ibid.* **12**: 307 (Sept.) 1934, Biomicroscopy of Limbus Corneae in Trachoma and Other Conjunctival Disease, *Am. J. Ophth.* **17**: 787, 1934.

80 de Rotth, A. Problem of Etiology of Trachoma, *Arch. Ophth.* **22**: 533 (Oct.) 1939.

81 Braley, O. E. Rickettsial Question in Trachoma, *Arch. Ophth.* **22**: 262 (Aug.) 1939.

82 Bengston, I. R. Question of Rickettsial Nature of Trachoma, *Am. J. Ophth.* **23**: 770, 1940.

the condition is comparatively rarely diagnosed, either because the patient does not seek medical attention owing to the mildness of the symptoms, or because the disease escapes detection. Thygeson and Mengert<sup>73</sup> reported the case of a gynecologist who was infected in performing a dilation and curettage and in whom conjunctivitis developed six days later; the secretions showing free initial and elementary bodies. After observation of the inclusions in the male urethra Lindner stated that the two viruses were identical and referred to the virus of inclusion conjunctivitis as the virus of paratrachoma. Inclusion conjunctivitis and inclusion urethritis heal without producing general immunity or neutralizing antibodies in the serums. Botteri and Gebb found the virus capable of passing through the pores of earthenware filters, Thygeson using an Elford collodion membrane of 0.6 micron pore diameter, observed the individual elementary body, of 0.25 micron diameter, in stained specimens, the initial body being 0.3 to 0.8 micron in diameter.

Morphologically the virus of trachoma and the virus of inclusion blennorrhoea (including swimming pool conjunctivitis) cannot be differentiated. Biologically it is possible that they are variants of the same virus, in analogy with the virus of variola and vaccinia. Virus research has resulted in the identification of a new clinical entity, nongonococcal inclusion conjunctivitis. Swimming pool conjunctivitis, often unilateral and similar to inclusion conjunctivitis, but without pannus formation or cicatrization, is due to the same virus infection probably taking place through contamination of stagnant water with urine of patients with inclusion urethritis. The inclusion conjunctivitis of the newborn is usually bilateral, in cases of unilateral infection the second eye becomes involved after six days or more. When pseudomembranes form, the possibility of scarification exists, as pointed out by Lindner, Aust and Lombroso, not as a result of an inherent tendency to scarring but as a sequel to the intense inflammatory process. Clinically there are changes of the follicular or papillary type, with adenopathy.

#### HERPES SIMPLEX

Long before the discovery of the virus origin of herpetic diseases which afforded differentiation of the virus of herpes simplex febrilis (corneae, cutis and genitalis) and that of herpes zoster, clinical ophthalmology had achieved a differentiation of these two forms of corneal lesions. In herpes febrilis the vesicular eruption, often accompanied by symptoms of involvement of the respiratory tract, is of short duration

and clears up without dense cicatrization. Conversely, the eruption of the cornea in herpes zoster, a sequel to infection of the nasociliary branch, is characterized by long duration, involvement of the stroma of the cornea, severe uveitis and formation of deep and dense scars.

The clinical picture of herpes febrilis corneae was clearly outlined by Horner,<sup>83</sup> in 1871, and his pupils Haab, Kendall, Wangler and Hagnauer subsequently defined it in minute detail. Other authors have proposed a different nomenclature for herpetic disease of the cornea. Keratitis dendritica myotica exulcerans (Emmert), keratitis ulcerea en sillon étoilée (Gillet de Grandmont), and keratitis ramiformis (Hansen and Grut) are examples, but these terms have not been accepted.

In 1873 Vidal demonstrated that herpes was infective, but little interest was taken in this fact until Grueter<sup>84</sup> produced herpes simplex in the cornea of the rabbit, proving the existence of a virus or virus-like agent and disproving the previously accepted theory of a trophic disturbance of the trigeminal nerve. The discovery of the transmissibility of the disease should doubtless be accredited to Grueter. Some authors have cited Loewenstein<sup>85</sup> or Loewenstein and Grueter. Loewenstein published his work before Grueter's and mentioned only briefly the latter's transmission of herpes to the cornea of the rabbit. Grueter achieved this in 1912, and his work represents the first clear positive evidence of the causation of herpes. He reported positive results from inoculation of the scarified cornea of the rabbit with material from a case of dendritic keratitis, passage from rabbit to rabbit and reinoculation from rabbit to man, and he noted that the inoculated animals were immune to revaccination with herpes. These observations were confirmed and extended to include all the varieties of herpes of the skin (Loewenstein) exclusive of herpes zoster. Forty-eight hours after the inoculation the scarified rabbit cornea revealed cloudiness with numerous small focal swellings. In the next two days purulent conjunctivitis and ulceration of the cornea became manifest. The local inflammation subsided in a few days, with residual corneal

83 Horner. Herpes Zoster Corneae and Herpes Febrilis Corneae, *Klin Monatsbl f Augenh* 9 172, 1871.

84 Grueter, W. Experimental and Clinical Studies of So-Called Corneal Herpes, *Klin Monatsbl f Augenh* 65 398, 1920, The Herpes Virus and Its Clinical and Etiologic Significance, *Munchen med Wchnschr* 31 1058, 1924.

85 Loewenstein, A. Experimental Studies on Virus of Herpes Febrilis, *Klin Monatsbl f Augenh* 64 15, 1920.

damage of variable degree. The scarified cornea of the rabbit became the classic culture medium for the inoculation of viruses. Only recently, Gallardo<sup>86</sup> reported that transmission is possible without mechanical insult to the corneal epithelium, by dropping or swabbing the material into the conjunctival sac. A later observation by Doerr proved that after nine days a certain proportion of the inoculated animals showed a lesion of the central nervous system, which manifested itself in forced turning to the infected side, paralysis of the rear extremities, convulsions and death. The route of extension after inoculation of the cornea is the retina, the optic nerve and the sensory divisions of the fifth and ninth nerves. The virus proved to be transmissible from rabbit to rabbit by the corneal or the intracerebral route.

In the early stage examination of the filtrations revealed no inclusions in the infected cells similar to Guarnieri bodies. This observation was contrary to the conclusion of Lipschutz<sup>87</sup> that the herpes virus was filtrable and belonged to the group of chlamydozoa and his report of numerous round, homogeneous and sharply outlined inclusions which filled the nucleus in the infected cells of the cornea. The inclusions were noted not only in the epithelial cells but in the fixed cells of the stroma, their presence denoting a nucleotropism of the virus. In Lipschutz' opinion, the inclusions represented reaction products of the cells to the invasion of the virus and belonged to the karyo-oikon group of chlamydozoa or strongyloplasms. The acidophilic nuclear inclusions occur in the epithelial cells of the cornea and skin. According to Goodpasture and Teague, they exist in all susceptible tissues of the infected animals. Nicolau and Kopciowska<sup>88</sup> concluded that the inclusion body was a closely packed colony of virus particles, not quite filling out the area rendered vacant by the peripheral accumulation of the chromatin. In rabbits, guinea pigs and mice, the central nervous system, next to the cornea, is most susceptible to the virus, however, other tissues are susceptible to a lesser degree, and cutaneous lesions can be produced by suitable strains. The external surface of the respiratory membrane (chorio-allantois) of the developing chick embryo is covered by ectodermal epithelium and reacts to the virus, but mesodermal tissues can be inoculated, too (testicular inoculation of rabbits).

86 Gallardo, E. Primary Herpes Simplex Keratitis, *Arch Ophth* **30** 217 (Aug) 1943.

87 Lipschutz, B. Chlamydozoa-Strongyloplasms, *Wien med Wchnschr* **71** 231, 1921.

88 Nicolau, S., and Kopciowska, L. Morphology of Herpetic Infrabacteria in Tissues of Experimentally Infected Animals, *Ann Inst Pasteur* **60** 401, 1938.

The virus can be preserved in neutral glycerin. The brain of infected animals contains the virus, and transmission from brain to brain is possible. The virus is quantitatively the same in all herpetic eruptions and is present in the serum and the spinal fluid of patients with herpes, in the saliva of patients with and without herpes and occasionally in the spinal fluid of persons who have not recently had herpes of encephalitis (Flexner).

The herpes virus has an ectodermal affinity, is relatively large, being 0.1 micron in diameter in filtration products (Elford, Perdrau and Smith<sup>89</sup>) or 0.1 to 0.3 micron in Levaditi strains, and filters with relative ease, particularly when suspended in broth. The filtrability was first proved by Luger and Landa,<sup>90</sup> in 1921. The various strains of the virus differ in virulence. The virus shows adaptation to animal species and to special tissues. Doerr suggested that the herpes virus may be identical with the virus of encephalitis.

Recovery from corneal or cutaneous inoculation in rabbits results in immunity for six months or longer, the serum and, to a lesser degree, the brain tissue show limited and irregular neutralizing power. In animals the herpes represents a typical virus infection, an extrinsic infectious agent producing the effect in susceptible animals and in susceptible tissues. It is a qualitatively identical agent, which is transmissible indefinitely. In man the condition is less clear, and Doerr expressed the opinion that it is not an exogenous, but an endogenous, infection, arising from the reaction of products of the cells to a virus-like agent under the influence of physiologic stimuli. Once the agent is produced, it will act on the cells as a true virus, but is only a derivative of the physiologically modified human cell.

Burnet and Williams,<sup>91</sup> who did not accept Doerr's explanation, undertook to prove the exogenous nature of herpetic infections, as having a direct origin in a preexisting virus. The virus remains latent after disappearance of the clinical symptoms, but it may become activated under the stimulus of trauma or fever and produce new lesions. The fact that herpetic lesions tend to recur at the same sites (lip, finger and cornea) points to the presence of vegetation in the affected cells, but certain investigators have stated the opinion that the virus persists in some part

89 Elford, W. J., Perdrau, J. R., and Smith, W. The Filtration of Herpes Virus Through Graded Colloidion Membranes, *J Path & Bact* **56** 49, 1933.

90 Luger and Landa. Etiology of Herpes Febrilis, *Ztschr f d ges exper Med* **24** 289, 1921.

91 Burnet, F. M., and Williams, S. W. Herpes Simplex. A New Point of View, *M. J. Australia* **1** 637, 1939.

of the nervous system, perhaps in the Gasserian ganglion, or in the mouth or the salivary glands

Herpes is an acute disease of infancy and early childhood 90 per cent of the population showing herpetic antibodies, which in all probability prevent the occurrence of herpetic stomatitis later Gundersen's<sup>92</sup> observation, based on 250 attacks of herpes in 225 patients, that the incidence of the disease was highest before the tenth year of life seems to be in accordance with that of Burnet and Williams, who expressed the belief that herpes is a disease of early childhood In my experience, dendritic keratitis in childhood is extremely rare, and in adults recurrence is always in the same cornea, a characteristic which apparently excludes the presence of virucidal antibodies Gallardo's<sup>86</sup> examinations showed that in cases of primary herpes of the cornea the serum did not contain neutralizing antibodies in the early stage (at the end of two or three days in 4 of 5 cases) In 17 cases of corneal herpes with a history of previous corneal or cutaneous eruptions, the antibodies were present at the onset The recurrence of herpetic lesions in spite of the presence of neutralizing antibodies points to the persistence of the virus within the susceptible cells The virus of herpes and that of epidemic keratoconjunctivitis are further differentiated by the long duration of the corneal manifestations in the latter disease and by the absence of a tendency to recur It should be mentioned briefly that Gundersen had 63 positive results in 180 inoculations and that in 3 cases the picture was that of disciform keratitis

It is interesting to note that the neurotropic quality of the herpes virus led von Szily<sup>93</sup> to study sympathetic ophthalmia He produced inflammation of the second eye in rabbits, but in 20 per cent of the animals the inoculation resulted in severe encephal meningitis Similar experiments were undertaken by Gifford and Lucie<sup>94</sup> and by Vellhagen<sup>95</sup> but the results can be considered only as transmission of the virus infection to the second eye, without its being connected with the causation of sympathetic ophthalmia in man In sympathetic ophthalmia the histologic picture is compatible with, if not suggestive of, a virus origin While the presence

of mononuclear elements, with a thick cuff around the vessel, testifies to a virus origin, the presence of eosinophilia points, rather, to an allergic factor<sup>76</sup>

#### HERPES ZOSTER

Herpes zoster, in its primary and secondary (symptomatic) form, is probably due to the same virus as that of herpes febrilis, the spread of the virus being distal, along the distribution of the nerve

The virus of herpes zoster has not been as extensively studied as that of other viruses, owing to lack of susceptible experimental animals The virus is possibly identical with, or at least closely related to, that of varicella, herpes zoster being the dermatropic and varicella the neurotropic manifestation of the same virus Thygeson,<sup>16</sup> in his exhaustive review, summarized the similarities of varicella and herpes zoster and mentioned the identity of the incubation periods and the cross agglutination and complement fixation reactions, the similarities in the histologic changes and in the inclusion and elementary bodies, the nontransferability and noncultivability of the viruses, the lasting immunity produced by both and the resemblance of the clinical pictures and the occasional simultaneous occurrence of the two conditions

#### MOLLUSCUM CONTAGIOSUM

Molluscum contagiosum was first described by Bateman, in 1817 Long before viruses were recognized, the large hyaline structures in the lesions of molluscum contagiosum, now identified as inclusion bodies, were described almost simultaneously by Henderson<sup>96</sup> and by Paterson<sup>97</sup> in 1841 The filtrable acidophilic cytoplasmic inclusions, which are microscopically visible, consist of an aggregation of minute elementary bodies, they were first described by Lipschutz,<sup>98</sup> who called them Strongyloplasmas, because viruses of this type are manifest as delicate, round bodies According to Lipschutz, Strongyloplasma hominis is the virus responsible for molluscum contagiosum The elementary body is 0.25 micron in diameter in Giemsa-stained films and is embedded in a matrix containing lipid elements The inclusion body is circular or pear shaped and is surrounded by a membrane Van

92 Gundersen T Herpes Corneae, Arch Ophth 15 225 (Feb) 1936

93 von Szily, A New Paths in the Experimental Research of Sympathetic Ophthalmia, Deutsche med Wchnschr 52 1598, 1926

94 Gifford S R, and Lucie, L M Sympathetic Uveitis Caused by the Virus of Herpes Simplex, Tr Sect Ophth, A M A, 1926, p 20

95 Vellhagen, K Experiments with Herpes Virus on Transmission of the Infection from One Eye to the Other Arch t Ophth 119 324, 1927

96 Henderson, W Notice on the Molluscum Contagiosum, Edinburgh M & S J 56 213, 1841

97 Paterson, R Cases and Observations on the Molluscum Contagiosum of Bateman, with an Account of the Minute Structure of the Tumours, Edinburgh M & S J 56 279, 1941

98 Lipschutz, B Diagnosis of Molluscum Contagiosum, Wien klin Wchnschr 20 253, 1907, footnote 17

Rooyen and Rhodes<sup>99</sup> demonstrated that the inclusion body can be removed from the cell by microdissection and that the capsule contains glycogen. The virus passes the Chamberland, Berkefeld, Berkefeld V and Pasteur-Chamberland L filters. The serum from patients with the disease contains no agglutinins, the absence of which may be attributed to the fact that the virus grows only in the superficial epithelial layers. That the virus is not transmissible to laboratory animals, not even to *Macacus rhesus* monkeys, suggests a high specificity of the virus with respect to species and tissue. Julianelle and James<sup>100</sup> confirmed the nontransferability of the virus to monkeys, rabbits and mice (by the intraperitoneal and the intracerebral route in the latter), but implantation in hens' eggs was followed in 2 out of 4 instances by infection of the chorioallantoic membrane, multiplication of the virus and the appearance of inclusion bodies.

Cutaneous transmission of molluscum contagiosum from man to man has been accomplished. The virus origin was established in 1905 by Juliusberg,<sup>101</sup> who demonstrated the transmissibility by material passed through Chamberland filters. The period of incubation after inoculations of filtered or unfiltered tissue extract varies from fourteen to fifty days, according to different authors. The inclusion bodies originally were thought to represent a parasitic protozoon (Lip-

schutz, von Prowazek). The virus does not produce immunity. The ocular manifestations are nodules on the margins of the lids, a follicular or, rarely, a papillary form of conjunctivitis, keratoconjunctivitis, with subepithelial infiltrates resembling the epidemic variety,<sup>102</sup> and actual tumor of the conjunctiva, or even of the cornea.

#### WART (VERRUCA VULGARIS)

Conjunctivitis, superficial keratitis and, in 1 case, a catarrhal type of ulcer were described by de Rotth<sup>103</sup> as complications of wart, with a tendency to heal promptly after removal of the lesion. The infectivity of warts was first proved by Variot and Jadassohn, and the filtrability of the virus through a Berkefeld N candle filter was demonstrated by Ciuffo, in 1907. Later, investigators found the virus filtrable through Berkefeld filters of all grades of porosity.

The spreading of warts by bleeding has long been known to the laity, before the infectivity was established scientifically. Despite numerous attempts, animal inoculations yielded definite results only with the transmission of laryngeal papilloma. Elementary bodies were not described. The increased eosinophilic granularity of the superficial layers often led to their being described as inclusion bodies. The inclusion bodies were said to be basophilic or eosinophilic, cytoplasmic or nuclear. Large granular eosinophilic bodies have been described by various authors, but their presence cannot be considered as proved, and further investigation is required. The nuclear inclusions are likewise questionable. The virus has not been cultivated.

#### 31 Lincoln Park

102 Lee, O. S. Keratitis Occurring with Molluscum Contagiosum, *Arch Ophth* **31** 64 (Jan) 1944.

103 de Rotth, A. Common Wart as an Etiologic Factor in Certain Cases of Conjunctivitis and Keratitis, *Arch Ophth* **21** 409 (March) 1939.

99 Van Rooyen, C. E., and Rhodes, O. J. *Virus Diseases of Man*, London, Oxford University Press, 1940.

100 Julianelle, L. A., and James, W. M. Molluscum Contagiosum of the Eye. Its Clinical Course and Transmissibility and Cultivability of the Virus, *Am J Ophth* **26** 565, 1943.

101 Juliusberg, M. Virus of Molluscum Contagiosum in Man, *Deutsche med Wchnschr* **31** 1598, 1905.



## Correspondence

### ANTERIOR PERIPHERAL SYNECHIAS IN EXPERIMENTAL ACUTE GLAUCOMA

*To the Editor*—In his interesting paper entitled "Development of Anterior Peripheral Synechiae in Experimental Acute Glaucoma" (ARCH OPHTH 31 481 [June] 1944), Dr M Uribe Troncoso compares the formation of peripheral synechia in experimental glaucoma produced by injection of serum or pure or defibrinated blood into the anterior chamber of animal eyes with the acute glaucoma of human eyes. He concludes that experiments with animals show that the first step in the production of this increase in tension was not the mechanical obstruction of the channels of outflow by the base of the ciliary body and the root of the iris but a disturbance in the normal outflow of aqueous. These conclusions cannot be applied to the condition designated as acute glaucoma in man. In the latter condition there is an anatomic predisposition, namely, shallowness of the anterior chamber, which is always present. In the animal eyes studied by Dr Troncoso the chambers were normal. I believe that this experimental condition might be compared more appropriately to the development of peripheral anterior synechias in certain cases of so-called secondary glaucoma associated with inflammatory increase of protein in the aqueous, but not to acute glaucoma.

Dr Troncoso also states in his conclusions that the "thickened processes pushed the root of the iris forward, made the anterior chamber shallow and produced an anterior peripheral synechia." This process cannot be compared to human acute glaucoma, in which there is no evidence of any decrease in depth of the anterior chamber before or after the attack. It is true that edema of the ciliary body and the root of the iris decrease the angle, but not the axial depth, of the anterior chamber.

In the early part of his paper Dr Troncoso refers to my previous work as reviving the theory that mechanical occlusion of the angle by peripheral synechias is the principal cause of acute glaucoma. This statement may cause misunderstanding, since I have always considered that peripheral synechia is secondary and that simple mechanical occlusion by approximation of the iris to the trabecula is the primary cause of the increased intraocular pressure in acute glaucoma. Peripheral synechias form only afterward, when edema and exudation from the ciliary body are present, during the congestive phase of this condition.

Again, Dr Troncoso refers to my series of 20 eyes, with shallow angles, in 6 of which mydri-

asis produced acute glaucoma, and states that in the 14 eyes in which mydriasis did not cause increased tension "the mydriatic did not produce any hypertension, although the dilation of the pupil undoubtedly narrowed the entrance to the chamber recess." In that paper (Sugar, H S. The Mechanical Factors in the Etiology of Acute Glaucoma, *Am J Ophth* 24:851, 1941) I pointed out that the angle cannot be blocked unless the combination of thickness of the iris, amount of dilation and shallowness of the angle is sufficient to produce mechanical blocking. Simple narrowing of the entrance is not enough. Mydriasis in that series of cases was not sufficient to produce the desired mechanical effect.

MAJOR H SAUL SUGAR, Medical Corps,  
Army of the United States

*To the Editor*—In his letter Major H Saul Sugar disagrees with some of my conclusions and objects to some of the interpretations I advanced as a result of my experimental work. Hence I consider it necessary to make certain explanations and to clarify my point of view.

Dr Sugar states that my experiments on animals "cannot be applied to the condition designated as acute glaucoma in man because in man there is an anatomic predisposition, namely, shallowness of the anterior chamber, 'which is always present, [while] in all animal eyes studied the chambers were normal.'" From the beginning I clearly stated in my paper that, unfortunately, there is as yet no means of reproducing experimentally the symptom complex designated as acute primary glaucoma in man. The injection of serum or pure or defibrinated blood into the anterior chamber is, in my opinion, the more physiologic approach to the experimental production of a sudden and great increase in intraocular pressure. Once this increase has developed, it is possible to ascertain the time of onset, the origin and the mechanism of formation of anterior peripheral synechia.

Dr Sugar states that an indispensable condition for the production of acute glaucoma is "always" a predisposing factor, shallowness of the anterior chamber. I believe that even in man this is not always a requirement for development of the acute attack. One of the most important contributions to ophthalmology made by gonioscopy has been to prove beyond doubt that a high intraocular pressure may coexist with an entirely open angle. I have described cases of glaucoma in which a tension of 40 mm of mercury or more coexisted with an entirely open angle and an anterior chamber of normal depth. These observations discredit the old theory of Knies



and Weber that the *primum movens* in the causation of hypertension is always the mechanical application of the root of the iris to the corneoscleral limbus

It is well known that subacute, or even acute, attacks may develop suddenly in eyes affected with simple glaucoma. It has been objected that in such cases acute hypertension, and not acute glaucoma, was the condition involved. Dr Sugar and other observers assert that an acute attack may be present without any symptoms of congestion and that congestion is not the characteristic feature of the acute exacerbation. This opinion is contrary to that of the majority of ophthalmologists. Periodic elevations of the intraocular pressure may exist with no congestion in cases of simple glaucoma, but when a true attack develops there is always a sudden and great increase of the pressure inside the eye. This compresses the intraocular veins, especially the venae vorticosae, and gives rise to congestion and secondary edema of the ciliary body and ciliary processes. The swollen processes compress the root of the iris against the trabeculum, so that the channel of outflow for the intraocular fluid is mechanically closed and thus another factor is added to the already high pressure.

Which condition is the cause of the primary sudden elevation of tension in the acute attack is not yet known, but it can be stated that when the causative factor is not sufficiently strong the attack is slight or prodromal. In cases of this type, the channels of outflow being normal, the level of tension falls quickly to normal, even when there is shallowness of the angle and the volume of the lens is probably greater. I have ascertained by gonioscopic examination that after a prodromal attack the angle of the anterior chamber remains open, either totally or partially. When the exciting factor is stronger and raises the intraocular pressure suddenly to a high level, inflammatory edema soon appears. The swollen processes compress the root of the iris against the sclera and produce an anterior peripheral synechia.

Dr Sugar states that in the acute attack in man "there is no evidence of any decrease in depth of the anterior chamber before or after the attack." This opinion is opposed to the accepted view. Dr Sugar probably supports this assertion by his direct measurements of the depth of the chamber. These, however, have not yet been confirmed. At any rate, he concedes that the edema of the ciliary body and the root of the iris makes for shallowness of the angle, which is the important point.

He fears my contention that he and other observers consider the mechanical closing of the

angle by peripheral synechia as the first step and the principal cause of the acute attack may lead to misunderstanding of his position. He adds that simple mechanical occlusion "by approximation" of the iris to the trabecula is the primary cause of increased intraocular pressure. These two statements differ only in their wording. The majority of ophthalmologists consider the application of the root of the iris to the trabecula as a peripheral synechia. This application, or agglutination, may be temporary if the iris is detached by the use of a myotic, or it may become permanent if the two membranes are bound together by connective tissue. The word "approximation" is misleading. It is only when the root of the iris comes in direct contact with the trabecula and covers it entirely that the channel of outflow is blocked. Dr Sugar himself states later that "simple narrowing of the entrance of the chamber is not enough."

the angle cannot be blocked unless the combination of thickness of the iris, amount of dilation of the pupil and shallowness of the angle is sufficient to produce mechanical blocking." I am entirely in agreement with him on this point. I merely indicated that in only 6 of his series of 20 eyes with shallow angles were these conditions met with and mydriatic glaucoma produced, while in the other 14 eyes the mydriatic did not give rise to elevation of tension. In my opinion, while mechanical blocking of the angle may "start" the cycle of symptoms of acute hypertension in some cases, in the majority the initial cause of the acute attack should not be ascribed to the mechanical occlusion of the angle of the anterior chamber.

I stated in my paper that while the anatomic differences between the angle of lower mammals and that of man are great, the experimental production of a sudden increase in tension was usually accompanied by congestion of the eye, edema of the conjunctiva and chemosis. In monkey eyes, the anatomic features of which are similar to those of the human eye, the same symptoms were produced. My aim was to determine the reaction of the eye to experimental hypertension of a high degree, to ascertain whether the anterior peripheral synechia was immediately or secondarily produced and, in the latter case, to determine the mechanism of its development.

I am obliged to Dr Sugar for bringing this important subject under discussion.

MANUEL URIBE TRONCOSO, M D,  
New York

630 West One Hundred and Sixty-Eighth Street

## Obituaries

---

SIR WILLIAM LISTER, M D

1868-1944

Sir William Lister died at his home in High Wycombe, Buckinghamshire, England on July 7, 1944. He was born on Nov. 4, 1868, the youngest son of Arthur Lister, F R S, an eminent botanist, and was a nephew of the great Lord Lister. He attended Cambridge University and then received his medical education at the University College Hospital, in London, and at Cambridge, where he graduated in 1892 and obtained the F R C S diploma in 1895. He was early drawn to ophthalmology, and he began work under Sir John Tweedy at Moorfields. Like so many eminent predecessors, Lister was curator of the pathologic museum at Moorfields before being elected to the visiting staff there. He also acted as ophthalmologic surgeon to the London Hospital. In 1914, at the onset of the first world war, he was asked to take charge of the ophthalmic arrangements for the Expeditionary Force in France. Mr Charles Goulden, in the August 1944 issue of the *British Journal of Ophthalmology* states that "the task of organizing the ophthalmic service of the British Armies in France" was an arduous one, but "by his persistence he ultimately overcame all difficulties and set up a most successful organization whereby not only was there an ophthalmic consultant available for each Army but surgical aid was obtainable at certain casualty clearing stations." His organization "was a great triumph, and it was achieved in the face of much opposition."

After the termination of the war Lister returned to the staff at Moorfields, where he became an active and most successful teacher in

the training of postgraduates in ophthalmology. In 1918 he gave a Hunterian Lecture before the Royal College of Surgeons on war injuries of the eye. Lister published important papers on interstitial keratitis, on retinal holes and on mustard gas burns of the eye. He was one of the first to discover that in retinal detachment the vitreous is always shrunken from one-third to one-half its former size, and in his paper on detachment of the vitreous, read before the International Congress of Ophthalmology in Washington, D C, in 1922, he drew attention to holes in the vitreous. He made several improvements in the instruments in constant use by ophthalmologists, and of these his perimeter was the most important.

He and Lady Lister were much interested in the Moorfields Eye Hospital and, in addition to other bequests, made a large donation for a convalescent home. At the English-speaking Congress in London in 1928 the American visitors will always remember the garden party given by Sir William and Lady Lister at the home of the Misses Alexander in South Kensington. In 1934 he was chosen consulting ophthalmologic surgeon to the King.

A man of the highest principles, of a modest and generous nature, Lister will long be remembered as a great clinician, a fine operator and an excellent teacher.

The material for this obituary was obtained from the *British Medical Journal* (2:130 [July 22] 1944) and from the *British Journal of Ophthalmology* (28:424 [Aug] 1944).

ARNOLD KNAPP

# Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

## Aqueous Humor

A CASE OF CAVERNOUS SINUS THROMBOSIS  
P D TREVOR-ROPER, Brit M J 1:255  
(Feb 19) 1944

A boy aged 14 years struck the region of his left eyebrow on a door handle. Two days later, as the area became sore, he attended the hospital, but nothing was apparent except a slight abrasion of the skin. The following day the eye began to protrude, and he had a temperature of 103 F. The condition rapidly grew worse, on the following evening the other eye was equally proptosed, and the next day the whole face was swollen. He was then vomiting, was incontinent and became semicomatose. This condition lasted one week, with the temperature about 103 F, he then gradually recovered. On the fifth to the eighth day tremors affected all the muscles of the face and the arm on one or both sides. The only changes in the fundus were slight engorgement of the retinal veins and possible blurring of the margin of the left optic disk. On his return to consciousness there was paralysis of the left side of the face which cleared in about a fortnight. There were stiffness of the right leg and paresis of the left external rectus muscle, which disappeared in a few days. Convalescence was delayed by mild basal pneumonia and a small subcutaneous orbital abscess. Vision was 6/5 in each eye.

Treatment included the administration of sulapyridine, which could be given only intramuscularly after the second day, and then oral use of sulfadiazine, 32 Gm the first week and 21 Gm the second week. Administration of 4 pints (1,890 cc) of 5 per cent dextrose in isotonic solution of sodium chloride, given as drip transfusions, was necessary while he was incontinent, vomiting and unable to take fluids by mouth.

In 1936 cavernous sinus thrombosis had a 100 per cent mortality. Since the advent of sulfonamide compounds, cures have been reported in 12 cases. In 3 cases, in conjunction with sulfathiazole, heparin was used for the prevention of extension of the clotting, in addition, staphylococcus antitoxin is recommended, even when the blood culture is sterile.

The author believes that the infection in this case reached the orbit from a nasal sinus through a fracture of the intervening bone, although this could not be shown on roentgenographic examination. (The abrasion of the brow was quite

sufficient to serve as a portal of entrance for the infection and was a much more probable source than the nasal sinus [abstracter] ) The meningeal irritation and residual palsies are a frequent accompaniment. Retinal changes have rarely been severe in the cases in which recovery occurred.

ARNOLD KNAPP

## Congenital Anomalies

COLOBOMA OF THE OPTIC NERVE. REPORT OF  
A CASE. T STEINBERG, Am J Ophth 26:  
846 (Aug) 1943

A man aged 20 had visual acuity of 6/60 in the left eye, which was unimproved by a correction of — 1 D sph — 1 D cyl, axis 55. There appeared to be a pseudo optic disk, about three times the size of the normal disk. Its center was conspicuously excavated, from — 6 to — 8 D.

The central portion was bluish gray and the periphery grayish white. The margins were sharply defined, the temporal side showing a thin, irregular ring of choroid pigment. The vessels appeared to emerge at the borders and bend sharply at the edges, corresponding to group 3 of Caspar's classification. No other lesions were present. The nasal field showed slight peripheral contraction and decided enlargement of the blindspot.

W ZENTMAYER

## Cornea and Sclera

THE PIGMENT OF THE KAYSER-FLEISCHER  
RING. R E ECKARDT, I H STOLZAR, A B  
ADAM and L V JOHNSON, Am J Ophth  
26: 151 (Feb) 1943

The authors give the following summary:

"1 Two cases of Wilson's disease, with typical Kayser-Fleischer rings in the corneas, are reported. A brief case history of each is given.

"2 The ashed corneas from these cases were subjected to spectrographic analysis. Abnormal cations common to both cases were zinc, copper, and iron. In addition, the cornea in one case showed the presence of silver and aluminum.

"3 No conclusions are drawn from these analyses, other than that the pigment deposited in the cornea in Wilson's disease may vary from case to case, even though showing certain similarities, and that this pigment may be more complex, at least in its cation composition, than was heretofore believed."

W S REESE

# CLEARING OF EDEMATOUS CORNEAS BY GLYCERINE D G COGAN, Am J Ophth 26 551 (May) 1943

Cogan has found the use of glycerin especially useful in examining patients who come to the clinic for the first time with acute attacks of glaucoma and in whom the steaminess of the cornea prevents adequate examination of the eye. If the cornea again becomes steamy, drops of glycerin may be instilled several times. The clearing effect lasts less than five minutes. He has found it to last longer if glycerin is used in tablet form. Glycerin tablets may be obtained by cutting up infant suppositories into appropriate sizes.

W ZENTMAYER

## Experimental Pathology

### THE REACTION OF THE RABBIT EYE TO NORMAL HORSE SERUM SENSITIZATION BY INTRADERMAL INJECTION T F SCHLAEGEL JR and J B DAVIS, Am J Ophth 26 785 (Aug) 1943

Schlaegel and Davis summarize their article and draw the following conclusions:

"Signs of uveitis were seen after 24 hours in the right eye of every rabbit previously sensitized by intradermal injection but were absent almost uniformly from the eyes of the control group.

"The uvea was the most involved membrane. It was infiltrated with lymphocytes, multinucleated giant cells, epithelioid-like cells, large mononuclears, and plasma cells.

"On the internal surface of the retina there developed an astrocyte type of gliosis that produced an additional inner layer almost as thick as the retina itself.

"Cellular infiltration in the control animals was less intense but of the same type as in those of series 1. It did not appear until 14 days had elapsed, but was constant thereafter.

"The histopathologic results of 'staphylophtheroid antigen' have been duplicated roughly by using normal horse serum.

"The microscopic picture obtained in the eyes injected with normal horse serum bears a close resemblance to that of sympathetic ophthalmitis."

W ZENTMAYER

## General Diseases

### SEVERE KERATO-IRITIS DUE TO BRUCELLOSIS SUCCESSFUL TREATMENT WITH BRUCELLA ABORTUS VACCINE J GREEN, Am J Ophth 26. 491 (May) 1943

Green is convinced that brucellosis is the true etiologic factor in many inflammatory ocular diseases. He cites the case of a young woman of rather low mentality who had well developed iritis, with subsequent deep vascular keratitis, in the right eye. The left eye became similarly

affected. Later, both eyes had iris bombe with secondary glaucoma. On clinical grounds, the condition was diagnosed by several consultants as tuberculous. Agglutination tests for *Brucella melitensis* and *Brucella abortus* gave negative results. A presumptive diagnosis of brucellosis was based on the positive results in the cutaneous and opsonocytophagic tests. A carefully regulated course of an oxidized *Br. abortus* vaccine (Foshay vaccine) led to remarkable clearing of both corneas and great diminution of vascularity. Both eyes were successfully operated on for the secondary glaucoma.

Green concludes that adequate laboratory tests for brucellosis should be made routinely in any case of a chronic inflammatory condition of the cornea, iris, ciliary body or uveal tract. Such tests should be made early in the course of the ocular disease. If other causes can be excluded, prompt and energetic treatment with a brucella vaccine may prove to be the means of checking the progress of the disease, and thus prevent blindness.

W ZENTMAYER

### OCULAR ROSACEA G WISE, Am J Ophth 26 591 (June) 1943

The present study of rosacea was undertaken primarily to evaluate the various etiologic possibilities in particular the theory that rosacea is due to riboflavin deficiency. The following conclusions are reached:

"Ocular rosacea occurs following facial rosacea and both are manifestations of the same disease.

"At present the fundamental cause of rosacea is unknown.

"Rosacea is not a manifestation of riboflavin deficiency.

"Previously considered causes of rosacea, such as gastrointestinal disturbances, focal infection, endocrine and other disorders, are not fundamental etiologically, but in some cases may be transient aggravating factors.

"Rosacea probably does not occur in the Negro race.

"Lowered gastric acidity is neither specific for rosacea nor nearly so frequent an accompaniment of it as has previously been thought. Its presence is of no special significance.

"Hyaluronic [acid] ester is not decreased in the cornea of the rat that has become vascularized due to riboflavin deficiency.

"The importance of secondary infection in cases of ocular rosacea has been neglected in the past.

"Except in the unusual and rare cases of severe ocular rosacea without secondary infection, most of the distressing symptoms and sequelae of ocular rosacea are due to secondary infection with staphylococci.

"The secondary infection in ocular rosacea can be controlled in almost all cases with 5-percent

sulfathiazole or sulfadiazine ointment, used locally several times daily

"Rosacea probably is due to some factor causing vasodilatation in the facial area"

W ZENTMAYER

### Hygiene, Sociology, Education and History

THE SCOPE OF PREVENTION IN OPHTHALMOLOGY IDA MANN, *Brit M J* 2:482 (Oct 16) 1943

The author, director of the Nuffield laboratory of ophthalmology, Oxford, England, after commenting on the recent publication by Marshall and Seiler (*Brit J Ophth* 26:337, 385, 434, 1942), states that though there were at the time of her report 74,000 blind persons in England and Wales, whose maintenance costs the state 4,500,000 pounds annually, nothing has been spent in planning the prevention of blindness. A possible reduction of ocular disease, Dr Mann believes, could occur mainly as a result of advances in three directions: improvement of the ophthalmic services of the country, education of the public on ophthalmic matters and further research on etiologic factors and therapeutics. The problem of the ophthalmic services of the country is linked with the problems of regional planning and medical education. As for the education of the public, the author suggests that education is needed at three levels: 1. Some biologic and physiologic instruction in schools should be obligatory, it should include an understanding of the mechanism of sight and the nature of binocular vision and of errors of refraction. 2. In adult life authoritative information should be available on such subjects as the care of the eyes and the nature of presbyopia. 3. Most especially, however, instruction is needed on protection of the eye in industry, since most minor injuries are due to the prevalent attitude toward safety-first measures and to ignorance of the possible effects of such injuries. The author believes that research requires greater collaboration between experts in the various branches of science. As advances in ophthalmology of recent years owe practically everything to basic discoveries in physics and chemistry—pharmacology and physiology also cooperating, laboratories would be desirable where physicists, physiologists, biochemists and pathologists, among others, could unite with ophthalmologists for the solving of given problems.

In conclusion, Dr Mann states that the problems of cataract and glaucoma will require the help of biochemistry for their solution and that uveitis must invoke experimentation in pathology, bacteriology and immunology. Venereal disease is yielding to chemotherapy, and myopia and the abiotrophies probably require genetic research for their understanding. The

question of injury includes experiments in the design of protective goggles and work on the best psychologic approach to insure their use.

ARNOLD KNAPP

### Injuries

TRANSIENT SLIT-LAMP APPEARANCE DUE TO CONCUSSION OF SMALL PARTICLES D D S STEWART and J P F LLOYD, *Brit J Ophth* 27:483 (Nov) 1943

A soldier received the "back fire" from the breech of a service rifle. This is described as a part of the exploding gases which escape backward, with which are conveyed very small particles of foreign matter, mainly fragments of incompletely burned charge. Biomicroscopic examination a little less than twenty-four hours from the time of the injury disclosed multiple minute foreign bodies, of various sizes, superficially embedded in the cornea, and many scattered areas of endothelial involvement. At the level of Descemet's membrane and the endothelium were minute gray plaques, disposed somewhat in the manner of the leaves of a formal laurel wreath, the central area being clear. The plaques gave the appearance of a grayish white substance (edema [?]) distributed around the endothelial cells. With a few exceptions at the periphery, these "wreaths" were circular and had an average diameter of about 2 mm, a superficial foreign body being seen to correspond to the center of each wreath. The phenomenon was still present thirty hours after the injury, but no trace could be found fifteen hours later. Vision was unaffected. It is suggested that the gray flecks were optical effects from local variations of the index of refraction.

The article is illustrated

W ZENTMAYER

### Lens

COMPARISON OF THE KERATOME-SCISSORS AND GRAEFE-KNIFE INCISIONS FOR CATARACT EXTRACTION C S O'BRIEN, *Am J Ophth* 26:508 (May) 1943

O'Brien summarizes his article and draws the following conclusions:

"1 The keratome-scissors incision for cataract extraction is simpler and safer than the Graefe-knife incision.

"2 Astigmatism is less after the keratome-scissors incision. In 110 consecutive extractions through keratome-scissor incisions, the astigmatism averaged 1.64 diopters, whereas, with a like number of Graefe-knife incisions, the astigmatism averaged 2.42 diopters.

"3 There was little difference in acuity of vision aside from the fact that a greater percentage of those with very high acuity were operated upon with the keratome-scissors technique."

W ZENTMAYER

**LANCASTER'S TECHNIQUE OF CATARACT EXTRACTION** K L ROPER, *Am J Ophth* 26: 540 (May) 1943

Roper describes and illustrates the instruments and technic employed by Lancaster in the performance of the operation for cataract extraction and gives the following summary and conclusions

"Dr Walter B Lancaster's technique of cataract extraction is described in detail. The importance of careful preliminary treatment and good anesthesia is stressed. Successive steps of his operation are described, the most important being his method of placing corneoscleral sutures before the section is made.

"Results in a series of 27 cases are reported wherein the author followed Dr Lancaster's technique exclusively.

"The high percentage of intracapsular extractions obtained, the low incidence of complications during and following surgery, and the low amount of astigmatism which resulted all seem to prove the merit of Dr Lancaster's technique."

The article is illustrated W ZENTMAYER

### Methods of Examination

**SOME CLINICAL APPLICATIONS OF FLUORESCENCE IN RELATION TO MELANOTIC PIGMENT** T L TERRY, *Am J Ophth* 26 536 (May) 1943

Terry gives the following summary of the clinical application of fluorescence to melanotic pigment

"Why hidden or obscured freckles in the skin or conjunctiva are so dramatically demonstrated under filtrated ultraviolet light in the true, rich brown color of melanin is not obvious.

"Relatively unpigmented tissues containing potentiality of pigmentation, such as unpigmented melanomata and unpigmented nevi, almost invariably appear to be heavily loaded with rich brown pigment under filtered ultraviolet illumination from the mercury-vapor lamp, a finding of perhaps real clinical value.

"Under conditions proper for fluorescence, unpigmented nevi usually appear too large to be removed completely, in many instances discouraging attempts at excision."

W ZENTMAYER

**OBJECTIVES OF ORTHOPTIC EXAMINATION AND TREATMENT** A LINKSZ, *Am J Ophth* 26: 552 (May) 1943

This article deals with the objectives of orthoptic examination and does not lend itself to abstraction

W ZENTMAYER

### Ocular Muscles

**ANISOCYCLOPLEGIA** S J BEACH, *Am J Ophth* 26: 522 (May) 1943

The term anisocycloplegia is coined to describe a caprice of cycloplegia such that one eye of a person is affected by the drug to a considerably greater degree than the fellow eye. Different methods of administration of the drug do not appreciably or consistently alter the situation. The phenomenon appears to be a property of the individual eye and to be independent of the method of administration. While it may be deceptive to any examiner taught to rely entirely on cycloplegics, it is a menace chiefly to ophthalmologists who are accustomed to base the prescription either on the unverified cycloplegic acceptance or the retinoscopic findings. The condition is revealed by the tests for depth of cycloplegia and by comparison with results of non-cycloplegic procedures.

W ZENTMAYER

### Retina and Optic Nerve

**DIATHERMY COAGULATION IN THE TREATMENT OF ANGIOMATOSIS RETINAE AND OF JUVENILE COATS'S DISEASE** REPORT OF TWO CASES J S GUYTON and F H MCGOVERN, *Am J Ophth* 26: 675 (July) 1943

The authors report a case of bilateral angiomatosis retinae in which diathermy coagulation gave gratifying results and a case of juvenile Coats's disease in which diathermy treatment apparently checked the progress of the disease.

In the first case, of early angiomatosis retinae of the right eye and advanced angiomatosis retinae of the left eye, the angiomatous masses were obliterated by diathermy coagulation. The sites of the angiomatous masses became scars, and the dilated retinal vessels were reduced in size. Vision was completely preserved in the right eye, and the ophthalmoscopic appearance of the left eye improved, although vision was not regained.

In the second case, of early juvenile Coats's disease of the right eye and complete blindness of the left eye, due to massive exudative retinitis, the left eye was enucleated because of early phthisis. Histologic examination of this eye showed a few areas of capillary proliferation in the retinal lesions, somewhat suggestive of angiomatosis retinae. The primary peripheral lesion in the retina of the right eye, which had steadily progressed in size for eleven months, was obliterated with diathermy punctures. The site of the peripheral lesion became a scar, edema of the disk and a subretinal exudate below the disk disappeared, and vision was completely preserved.

W ZENTMAYER

## Vision

TEST CHARTS REPRESENTING A VARIETY OF VISUAL TASKS M LUCKIESH, Am. J Ophth 27:270 (March) 1944

Luckiesh points out that contrast sensitivity, or the ability to see differences in brightness, is an important factor in seeing and that visual acuity, as measured by the common black on white chart, has gross limitations when applied to everyday seeing

W. S. REESE

DEFECTIVE NIGHT VISION AMONG SOLDIERS. DARK ADAPTATION RESULTS AND THEIR USE IN DIAGNOSIS I C MICHAELSON, Brit J. Ophth 28:140 (March) 1944

The purpose of the investigation was the determination of (a) the reliability of the Koch dark adaptometer, (b) the normal values for minimum form and light senses on the instrument and (c) the minimum form and light senses in subjects complaining of defective night vision, and the arrival at a differential diagnosis between psychogenic and organic defects in night vision

The following conclusions were reached

"The normal minimal light and form senses vary, but together afford sufficient if not a complete measure of the individual ability to see in the dark

"Cases of defective night vision have a poor minimum form sense. Many individuals without defective night vision have a poor minimum form sense

"Measurement of minimum light sense after three minutes' dark adaptation in cases of defective night vision does not appear to have much diagnostic significance

"Measurement of minimum form sense after three minutes' dark adaptation in cases of defective vision does appear to be diagnostically useful. There are indications that in such cases a poor minimum light sense is associated with organic disturbance, and a good minimum light sense with functional disturbance, as the cause of the defective night vision. Although the groups examined are not large, the data are suggestive and sufficient to indicate further investigations and tentative measures in treatment and disposal

"Dark adaptometers which measure the minimum form sense and not the minimum light sense have a limited usefulness for two reasons. First, there is a great variation in the minimum form sense among the non-complainers of defective night vision, and secondly, such instruments cannot help in the discrimination between psychogenic and psychogenic defective night vision in the manner detailed above. It cannot be over-emphasized that this differential diagnosis is one of the main pre-occupations of oculists in-

vestigating complaints of defective night vision among large groups of people"

W ZENTMAYER

## Therapeutics

TREATMENT OF OCULAR INFECTIONS WITH PENICILLIN G T WILLOUGHBY CASHELL, Brit M J 1:420 (March 25) 1944

The author finds that penicillin holds an important place in the treatment of ocular infections, such as acute conjunctivitis, blepharitis, corneal ulcer, perforating corneal injury and dacryocystitis. The remedy is found effective in cases of infection with *Staphylococcus aureus* and the hemolytic streptococcus, pneumococcus and gonococcus. The optimal strength is 500 oxford units per cubic centimeters, used in the form of drops or ointment. The substance is applied frequently at first, and then the frequency is reduced after the acute stage. Irrigation of the anterior chamber can be carried out with a solution of the drug in certain cases in which the infection has taken place through a perforating wound. It should be remembered that the penicillin loses its potency after fourteen days, and the solution should be stored in a refrigerator. The results in cases of the following conditions are briefly described: blepharitis, 20 cases, acute conjunctivitis, 10 cases, corneal ulcer, 10 cases, perforating injury, 14 cases, and dacryocystitis, 3 cases. A report of cultures and suggestions for dosage are made

ARNOLD KNAPP

## Toxic Amblyopia

THE OCULAR PATHOLOGY OF METHYL ALCOHOL POISONING W H FINK, Am J Ophth 26:694 (July), 802 (Aug) 1943

A comprehensive survey of the literature, a series of animal experiments and a report of 3 cases of fatal outcome are used as a basis for formulation of a more definite concept of the process and the nature of the pathologic changes in the eye associated with methyl alcohol poisoning

As a result of this study certain facts were evident

There exists an uncertainty concerning the action of methyl alcohol on the eye. The ocular tissues show characteristic pathologic changes

*Choroid*—A study of the microscopic data available indicates the presence of vascular congestion and edema, with little evidence of an inflammatory reaction

*Retina*—The toxic effect first makes itself evident in the ganglion cells. Then the inner nuclear layer degenerates, later the outer nuclear layer and, finally, the layer of rods and cones. It was



observed that if the layer of ganglion cells was greatly changed, other elements of the retina were also considerably affected. The general picture of changes in the retina, in addition to the degenerative process, is that of dropsical saturation.

*Optic Nerve*—There is definite evidence that degenerative changes occur in the optic nerve. Signs of edema accompany these degenerative changes to a variable degree.

The various ocular changes are similar, and all the affected tissues become involved simultaneously. Because of its delicate tissue, the reaction is more evident in the retina than in the nerve. Pathologic changes are fundamentally degenerative and occur as the result not only of the action of a toxic substance but of a metabolic disturbance due to the toxin.

The general observations at autopsy indicate pathologic changes of much the same type as those seen in the eye.

Methyl alcohol is broken down into other chemical substances, and one or more of these may be the cause of a toxic reaction greater than that caused by methyl alcohol itself. The pathologic change is the result of the direct action of the toxic substance on the tissues. The toxic substance produces a degenerative change in the tissue, especially the highly differentiated tissue, such as the cells in the retina and, to a lesser degree, the nerve fibers. That this is not an inflammatory change is evident from the absence of an inflammatory reaction. Edema of the nerve tissue and supporting tissue is the result both of irritative reaction of the tissue to the toxic substance and of the degenerative process.

W H FINK

# Society Transactions

EDITED BY DR W L BENEDICT

---

## COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

WARREN S REESE, M D, *Chairman*

GEORGE F J KELLY, M D, *Clerk*

*Jan 20, 1944*

### Intraocular Pressure and Its Relation to Retinal Extravasation DR JOSEPH IGRSHEIMER, Boston

This paper was published in full in the July issue of the ARCHIVES, page 50

### Marcus Gunn Phenomenon. DR EDMUND B SPAETH and DR JAMES S SHIPMAN

Two cases of the Marcus Gunn phenomenon were presented. In the first case the eyeballs were completely immobile, owing to surgically demonstrable fibrosis of all the extraocular muscles. The levator palpebrae superioris muscles, however, were noted at operation to be normal. Elevation of the lids in this case was bilateral and was associated with both opening and closing of the jaws. In the second case the phenomenon was unilateral. The classic picture of elevation of the right lid associated with action of the contralateral pterygoid muscle was present.

The cause and the theories connected with the development of this syndrome were discussed, the cases were illustrated by moving pictures, and the operation for correction of the syndrome was described.

#### DISCUSSION

DR F C GRANT: The pathways over which the afferent fibers pass to produce this phenomenon are so shrouded in mystery that it is unnecessary to discuss them. I cannot add much to what Dr Spaeth has said. Dr Lewy and Dr Groff, at my suggestion, did some work on this subject which seemed to indicate that the first division of the trigeminal nerve is concerned with the phenomenon to a considerable degree, but these experiments were not nearly as conclusive as we had hoped. I was much interested in having the opinion of an ophthalmologist on the treatment of this condition.

About five years ago my associates and I had a patient who presented the same symptoms as did Dr Spaeth's second patient, with elevation of one eyelid on contralateral movement of the jaw, a condition suggesting that the innervation of the pterygoid muscle on the same side was

always involved, for when that muscle was moved there was a corresponding elevation of the eyelid. In our groping neurologic way, we hypothesized that if the movements of the pterygoid muscle were interfered with, and it was impossible for the patient to move his jaw to the opposite side, the upward movement of the lid might thereby be prevented.

(Slide) When the patient moved his jaw to the right or when the mouth was opened in the midline, the right eyelid was immobile. The full face view shows the Gunn phenomenon, namely, a slight increase in the size of the palpebral fissure on the right side.

(Slide) Acting on the idea that if the movement of the pterygoid muscle on the affected side could be prevented the elevation of the lid on that side might be abolished, we blocked the third division of the fifth nerve on the right side with procaine and found that the patient could not move his jaw to the left, evidence that the motor root was paralyzed and that he had no upward movement of the eyelid. On reinforcement of the procaine with alcohol, 95 per cent of the function of the pterygoid muscle was lost, and he still could move his jaw about  $\frac{1}{4}$  inch (0.6 cm) to the left. With that movement, or effort, he still had the spasm of the eyelid. We then cut the third division of the right fifth nerve, together with the motor root. We got into serious trouble, for the patient had a postoperative hemorrhage that almost cost him his life. As a result of this complication, he had complete paralysis of the motor fifth nerve, and with that degree of paralysis he could not move his jaw to the left. In consequence, he had none of the previous associated movement. He recovered completely from the paralysis of the third and seventh nerves. The slide shows the result about eight months after operative intervention. There was slight evidence of the oculomotor weakness, but it was impossible for him to move his jaw to the left. Even with forcible movement of the jaw, there was none of the associated movement which had accompanied the contraction of the pterygoid muscle prior to operation.

Frankly, I do not know that I advise operative treatment of such a condition, especially if it may involve the possible hazards consequent to postoperative hemorrhage. Fortunately, this is an uncommon complication.

If there is an ophthalmologic surgical measure to offer such a patient, I think it preferable to the surgical procedure we attempted in this case. Our only excuse for operating on this patient was our

finding in the literature 100 cases of the Marcus Gunn phenomenon, in none of which any attempt had been made to correct the associated movement

DR WILLIAM ZENTMAYER Syndromes showing anomalous associated movements of the muscles of the face and of the eye have been classified by Friedenwald as follows (1) contraction of the levator palpebrae superioris muscle with movement of the jaw or with swallowing, (2) contraction of the orbicularis muscle in association with movement of the jaw, or contraction of the various facial muscles after facial paralysis, and (3) contraction of the levator palpebrae superioris muscle in association with abduction or adduction of the eye To these, I should add contraction of the frontalis muscle in association with abduction of the eye

The committee appointed by the Ophthalmological Society of the Royal Kingdom to report on Gunn's case stated the opinion that the phenomenon was to be explained by innervation of the levator palpebrae superioris muscle both from the nucleus of the third nerve and from the external pterygoid portion of the nucleus of the fifth nerve

In Harlan's case, reported before this section, rapid winking of the left eye during mastication, which gave the impression of blepharospasm, was an acquired condition, following an attack of typhoid, in a child aged 4 years

According to Harman and Topolanski (*Wien med Bl*, 1898), elevation of the alae of the nose accompanied normal blinking of the eyes in 20 per cent of persons examined Harman explained the Gunn phenomenon as representing an atavistic anomaly In the shark, for example, the fifth and seventh nerves are so closely associated that they are called the "facial complex"

Fuchs has described a syndrome in which the upper lid is raised in attempts at adduction and falls in abduction of the eyeball The reverse of this may also at times be observed Usually there is associated ptosis, and there may or may not be paresis of the internal rectus muscle Fuchs assumed that the excessive nerve energy which is supplied to the paralyzed nerve overflows into the neighboring nuclei

My own case of contraction of the frontalis muscle associated with abduction of the eyeball occurred in a man aged 20, with hyperopia and esotropia of 12 degrees His right eye was the fixing eye There was some limitation of the outward excursion of the left eye As the object of fixation was carried to the left, the movement of the left eye stopped when the object reached the midline, and the elevation of the left brow began as soon as abduction started and reached its maximum when the eye, by forced action, reached almost the external canthus There was no accompanying elevation of the lid or widening of the palpebral fissure There was neither

ptosis nor palsy of any of the ocular muscles Dr Weisenburg could detect no organic disease of the nervous system He made a moving picture of the patient and exhibited it before the Philadelphia Neurological Society

Wilbrand and Sanger (*Die Neurologie des Auges*, Weisbaden, J F Bergmann, 1900, vol 1, pt 1, p 57) reported a case very similar to my own

DR FRANCIS HEED ADLER In the present state of knowledge it is probably fruitless to suggest another explanation of this interesting condition It is curious, however, that no one has called attention to the possibility of a cortical or subcortical site of the lesion It is well known that in the vast majority of cases this phenomenon is associated with congenital ptosis None of the ocular muscles are represented individually in the frontal cortex except for those of the lid The levator palpebrae muscle is represented in the foot of the second frontal convolution adjacent to the representation of the muscles which move the jaws

Therefore, a lesion or absence of development of the cells in this area might easily account for this phenomenon At present, however, there is no evidence on which to base such a hypothesis

DR JAMES S SHIPMAN I saw the first patient whom Dr Spaeth presented, and I asked Dr Spaeth for a consultation He at once made a diagnosis and suggested the operative procedure which followed There is a question in my mind whether this procedure will produce permanent results As Dr Spaeth pointed out, the Marcus Gunn phenomenon is congenital, and the pseudo Graefe phenomenon is acquired However, the cause of the pseudo Graefe phenomenon is often the same condition as that produced by the operative procedure followed in this case, i e, laceration of the fibers to the levator muscle by trauma, with production of ptosis, and, later, regeneration of the nerve fibers to that muscle Abnormal movements may develop, for example, when the patient is looking down, the eyelid moves up My associates and I had a case of this type not many months ago

In Dr Spaeth's opinion, the basis of the Marcus Gunn phenomenon is a misdirection or an abnormal regeneration of nerve fibers The question is whether this patient will still present the same appearance three or five years from now that he has at present Before Dr Grant gives the ophthalmologists too much credit for the surgical cure of the Marcus Gunn syndrome, a few years should be allowed to elapse

DR EDMUND B SPAETH I appreciate the discussion on these cases Dr Shipman and I will present later a moving picture of the surgical procedure The longest period that the correction has been, and still is, maintained is a bit over four years Apparently, the correction is permanent I see no reason to doubt the permanence of these cures

Dr Grant's demonstration of the afferent pathway is convincing. I was interested in Dr Adler's comment. In my opinion, however, the cause of the Marcus Gunn phenomenon is not cortical stimulation, even though such a relation was indicated by Walsh's patient, who showed elevation of the lid when he became interested in an attractive member of the opposite sex, and by the second patient presented tonight, who had elevation of the upper lid when she became angry.

#### Precipitous Development of Optic Neuritis and Cataracts Associated with Hypoparathyroidism: Report of a Case DR WALTER I LILLIE

A case of bilateral optic neuritis and precipitous formation of cataract associated with postoperative hypoparathyroidism is presented. Ophthalmologically the case presented many interesting features.

1 The patient had had mild exophthalmos since the age of 10 years, and this had not changed in character during the entire course of the condition under discussion.

2 Blurring of vision associated with acute bilateral optic neuritis developed precipitously two months after thyroidectomy, but well in advance of any of the clinical signs, such as dermatitis and tetany associated with convulsions. 3 At the time of the first examination at Temple University Hospital, the lens in each eye showed only a few small, discrete opacities in the cortex anterior to the posterior capsule. Opacifications were of so minor a degree that examination of the fundus was not interfered with in either eye. Edema of the disk was visible with the ophthalmoscope. Ocular examination at this time revealed a classic optic neuritis syndrome.

4 The rapid development of cataracts to maturity and hypermaturity in the course of ten days during the patient's stay in the hospital is of great interest. Unfortunately, it prevented any examination of the fundus to determine the response of the optic neuritis to general treatment.

5 After successful extraction of the cataract in each eye, the fundus and the visual acuity were normal.

#### DISCUSSION

DR CHARLES L BROWN This patient's general condition was complicated, and of course, was associated with an extensive metabolic disturbance. I am inclined to think that not only severe chronic hypoparathyroidism but diminution in the function of the thyroid was involved. There was reason to believe that a nutritional deficiency also entered into the picture.

The last-mentioned point is not clearly understood, but it is apparent in other cases that have been reported. I am thinking particularly of a case which Dr Norman Learner and I reported (*J Clin Endocrinol* 2:261 [May] 1943), in

which we were able to demonstrate evidence of nutritional deficiency, especially in vitamin B. In this case, we also had evidence that vitamin D deficiency might play a part. Our patient had cutaneous manifestations, which became evident during the part of the year that this patient was not exposed to the usual amount of sunlight. It is interesting that many of the ectodermal changes that have occurred in connection with postoperative thyroid and parathyroid conditions seem to have been particularly prevalent in patients who were operated on between January and May. The hypoparathyroid state suggests disorders associated with calcium and phosphorus metabolism. How much this widespread metabolic disorder has to do with the formation of cataract and with the occurrence of other changes in ectodermal tissue one can only speculate.

It is not rare for cataract to occur as a manifestation, or feature, of chronic tetany. It is apparent from reports in the literature that cataract was recognized as being frequently associated with the nutritional tetany of young adults. Authors who described such cataracts called attention to the characteristic subcapsular distribution of these opacities. There has been indication that cataracts develop rather rapidly. In a case reported by Emerson, Walsh and Howard (*Ann Int Med* 14:1256 [Jan] 1941) cataract was said to have developed bilaterally, with complete blindness within four and one-half months. An interesting, and perhaps significant, point in Dr Lillie's case is the rapid appearance of the cataract—within ten days, while the patient was under his observation. It is interesting that dihydrotachysterol with calcium was an effective therapeutic agent in restoration of the calcium-phosphorus metabolism to normal. It would have been interesting to see whether this substance would have impeded the progress of formation of these cataracts if they had not been formed so rapidly.

I have never understood the exact nature of the increased intracranial pressure, together with the excessive formation of spinal fluid, in this case.

#### Foster Kennedy Syndrome with Fusiform Aneurysms of Both Internal Carotid Arteries. DR I S TASSMAN

This article was published in full in the August 1944 issue of the ARCHIVES, page 125.

#### DISCUSSION

DR BERNARD J ALPERS It would have been instructive if Dr Tassman had stated the difficulties experienced by a group of representative oculists in determining whether a Foster Kennedy syndrome was actually present in this case. There was considerable difference of opinion concerning the presence of optic neuritis in the

one eye and the existence of edema That, I think, is an important point

The feature of the greatest interest in this case is the so-called Foster Kennedy syndrome Two problems always develop in a consideration of the possible presence of this syndrome The first is that some one sooner or later raises the question of nomenclature and states that the condition is not the Kennedy syndrome at all

The second point is that the thinking about this syndrome has become largely oriented toward a diagnosis of tumor If one could find some other way of describing the pathologic picture, such as alternating edema and atrophy, ideas with regard to the causal factors might not be so fixed There is no question that a tumor in the suprasellar region is frequently present with this syndrome, but it is not so often recognized that the condition may be associated with aneurysm and arteriosclerosis of the vessels of the circle of Willis My associates and I recently had a case of a typical Foster Kennedy syndrome, with edema in one eye and atrophy in the other The patient had an injury to the head and later headache and loss of visual acuity developed first in one eye and later in the other The diagnosis was that of tumor He had a central scotoma in one eye and a field defect in the other A pneumoencephalogram revealed nothing significant Operation disclosed arachnoiditis with firm adhesions covering the optic chiasm and both optic nerves Because there seemed to be bulging over the third

ventricle, this area was explored, but nothing was seen in it It can be stated without hesitation that the syndrome in this case was due to arachnoiditis It is well to recognize that as more cases of this type of syndrome are encountered, more causes will be evident

DR W I LILLIE (Four lantern slides, illustrating various vascular anomalies of the anterior portion of the circle of Willis, were shown )

These vascular anomalies push the optic nerves upward and forward against the bony roof of the optic canals This continued pressure produces the typical prechiasmal syndrome described by Dr Tassman The operative procedure for relief of pressure is restricted to removal of the bony roof of the optic canal, as the vascular anomaly usually prohibits any surgical intervention

DR I S TASSMAN With regard to the differential diagnosis of papilledema and optic neuritis, to which Dr Alpers referred, the diagnosis of optic neuritis in the right eye was made in her home town I never believed that the condition in the right eye was anything other than papilledema, particularly in view of the presence of good central vision in that eye If it had been optic neuritis, central vision would have been much less than it was found to be—practically normal

Further, there was almost complete absence of any signs of inflammation about the nerve head or the vessels

---

## News and Notes

---

### GENERAL NEWS

**Annual Postgraduate Course, University of Virginia Hospital**—The eleventh annual postgraduate course will be held at the University of Virginia Hospital, in Charlottesville, Va., on Dec 5, 6, 7 and 8, 1944 The ophthalmologic program will be given on December 7 and 8, under the direction of Dr Edward W Burton, who is in charge of the section of ophthalmology The invited faculty will include Dr James W White, of New York, who will speak on muscular anomalies, Dr Paul A Chandler, of Boston, who will give lectures on disorders of the lacrimal passages, glaucoma and cataract, Dr Wilfred E Fry, of Philadelphia, who will lecture on diseases of the optic

nerve, and Dr Wendell L Hughes, of Hempstead, N Y, who will speak on repair of lacerations of the lid and reconstruction of the socket and of the lower lid

---

### CORRECTION

In the article by Dr Richard Waldapfel entitled "Infection of Lymphoid Tissue of the Pharynx and of the Conjunctiva," in the April issue (*ARCH OPHTH* 31 331-333, 1944), the *D* and the *B* in the legend under the picture on page 332 are reversed, in other words, in the third line of the legend *D* (case 1) should read *B*, and in the eighth line *B* (case 2) should read *D*

## Book Reviews

**Cataract and Anomalies of the Lens Growth, Structure, Composition, Metabolism, Disorders and Treatment of the Crystalline Lens** By John G. Bellows, M.D., Ph.D. Price, \$12 Pp 624, with 208 illustrations and 4 colored plates St. Louis C. V. Mosby Company, 1944

This book consists of 624 pages, of which about 291 pages comprise the text. There are excellent illustrations, a good index of subjects and a separate index of authors. At the end of each of the ten chapters there is a complete list of references, with titles. The foreword is by the late Dr. Sanford R. Gifford, to whose memory the book is dedicated.

Chapter I, consisting of about 28 pages of text, is ambiguously entitled "The History of the Crystalline Lens." It describes the evolution of knowledge of the lens from 2250 B.C. to modern times. Accommodation and the optical properties of the lens are not dealt with at length anywhere in the book, but in this chapter more than a page is given to prove that accommodation depends on change in shape of the lens.

Chapter II deals with the embryonic development of the lens in lower animals and in man and includes a mathematical consideration of the growth of the lens. It also deals with induction and regeneration of the lens, including formation of secondary cataracts and Elschnig bodies.

Chapter III deals with the structure of the lens in lower animals and in man. Neither the embryonic nor the adult nucleus is described as such, although they are referred to in later chapters.

Chapter IV deals with the chemical composition of normal and of cataractous lenses and with the immunologic properties of the lens. Phacoanaphylactic endophthalmitis is discussed somewhat at length, but its histologic characteristics are not described. It is astonishing that since the discovery of this condition, twenty-two years ago, nothing of definite clinical value has emerged from the enormous amount of investigative work referred to in this and in the next chapter.

Chapter V deals with the metabolism of the lens and with capsular permeability. These are subjects of the author's personal investigation, but he does not emphasize his contributions.

Chapter VI is entitled "Developmental Defects of the Crystalline Lens." It includes consideration not only of malformations of the lens, congenital aphakia and ectopia lentis, which are certainly developmental defects, but also of such conditions as coralliform, zonular and tetanic cataracts, which are chiefly dependent on metabolic disturbances.

Chapter VII deals with cataracts due to radiant energy, electricity, deficiency of vital constituents and toxins. The author concludes that it is unlikely that exposure to ultraviolet light is significant in the causation of senile cataract but seems to accept Vogt's contention that glassblowers' cataract (heat cataract) is due to specific action of infra-red rays.

Chapter VIII deals with cataracta complicata, cataracts due to trauma and displacements of the lens. Two pages are given to a discussion of siderosis of the lens. The author does not mention the fact that the deposits in the capsular epithelium tend to occur in the form of two rings, one behind the pupillary border and the other at the place where the iris leaves contact with the lens. He mentions von Hippel's explanation of siderosis but does not give it fully, and states that the best explanation is that of Ito. To the reviewer, von Hippel's hypothesis is the more satisfying for it explains why the iron granules are deposited chiefly in certain cells, notably in the epithelial cells of the capsule, in the cells of the pigment epithelium and the unpigmented layer of the pars ciliaris retinae and in the cells of the dilator iridis.

Chapter IX deals with cataract due to endocrine dysfunction, including diabetic cataract, cataracta parathyreopriva and the cataracts associated with dystrophia myotonica, hypothyroidism, mongolism and dermatologic disturbances.

Chapter X is concerned with senile cataract. Here the pathogenesis of this form of cataract is separately discussed. Considerable repetition could have been avoided if the few additional facts mentioned in this connection had been incorporated in chapters VIII and IX. The pathologic histology of senile cataract is inadequately described and is not illustrated at all. The author does not discuss, or even mention, the anterior capsular cataract often associated with senile and other types of cataract and hence does not point out the remarkable fact that the capsular epithelium can produce tissue closely resembling, if not identical with, mesoblastic connective tissue. He, also, does not point out that a morgagnian cataract can cause glaucoma or, by its spontaneous rupture, produce characteristic intraocular inflammation, with disastrous consequences. The title of a subsection in this chapter is "Is the Control of Cataract Possible?" The author does not definitely answer this question, but from the facts presented the reviewer concludes that no non-operative treatment that will prevent senile cataract or delay its progress has yet been proposed. The author states, without dissenting, that Schoen and Jackson "emphasize the fact

that strain, particularly during accommodation, alters the lens nutrition in some manner, producing a cataract." The reviewer questions the "fact" and suggests that the "strain" may even tend to prevent cataract by improving the nutrition of the lens. About 10 pages are given to the operative treatment of cataract and another 10 pages to postoperative complications. These two presentations are excellent so far as they go but are too incomplete to be of great value.

The format of the book is excellent. The text is clear and well arranged. It is so well worded that it is surprising to find "intraocular tension" invariably used instead of the correct term "intraocular pressure."

It is to be noted that the criticisms made in this review are comparatively unimportant and relate chiefly to omissions. With respect to the value of the book as a whole, the reviewer concurs in the opinion expressed by Dr. Gifford in the foreword: "Certainly this material cannot be found elsewhere in a single volume or in many volumes. There seems to be no doubt he has produced an exceedingly interesting and important work, one which will take its place as the authority on the crystalline lens."

F. H. VERHOEFF

**Intracranial Arterial Aneurysms** By Walter E. Dandy. Price, \$2.50. Pp. 147, with 55 illustrations and 6 charts. Ithaca, N. Y.: Comstock Publishing Co., Inc., 1944.

As a measure of the progress of neurosurgery in the last thirty years, it may be recalled that all knowledge on the localization and surgical treatment of tumors of the brain in 1914 could easily have been printed in a volume the size of this one, which does not discuss even all tumors of blood vessels (angiomas are not considered) but considers only intracranial aneurysms.

Ophthalmologists have become familiar with the ocular symptoms of intracranial aneurysms through the paper by Walsh and King (Walsh, F. B., and King, A. B. *Ocular Signs of Intracranial Saccular Aneurysms*. *Experimental Work on Collateral Circulation Through the Ophthalmic Artery*, *ARCH. OPHTH.* 27:1 [Jan.] 1942). The material for that paper was to a great extent derived from Dandy's series, and there is therefore a certain similarity between the description by Walsh and King and that in the present book. One finds again those curious denervation phenomena referable to degeneration of the third nerve and the anomalous movements of the eyeball and upper lid due to a misdirection of the regenerated fibers. At a certain stage of regeneration of a paralyzed third nerve, an Argyll Robertson pupil has been observed. When the aneurysm is large enough, papilledema may result, but in some patients retinal hemorrhages have been observed without papilledema—large, round, subhyaloid hemorrhages, thought to be pathognomonic of sub-

arachnoid bleeding and of an aneurysm on the same side. An anterior aneurysm is of course apt to bring pressure on the visual pathway.

The following symptoms are most frequently associated with aneurysm in various locations:

1. Internal carotid artery in the carotid canal: pain, severe and sudden, in the region of the eye and the frontal area, often associated with paralysis of the third nerve, involvement of the trigeminal nerve, paralysis of the fourth and sixth nerves, direct pressure on an optic tract or an optic nerve, and occasionally on the chiasm, and exophthalmos, if the aneurysm is large enough to erode the walls of the sphenoid fissure and push the orbital content forward.

2. Intracranial portion of the internal carotid artery:

(a) Diffuse dilatation of the trunk of the artery: homolateral primary optic nerve atrophy.

(b) Small sacculated aneurysm proximal to the origin of the branches: paralysis of the third nerve.

(c) Aneurysm of the internal carotid artery at or near its branches: paralysis of the third nerve, retinal hemorrhages without papilledema.

3. Anterior cerebral artery and anterior communicating artery: pressure on the optic nerves and optic chiasm, paralysis of the extraocular muscles in some cases.

4. Middle cerebral artery: subhyaloid hemorrhages of the retina without papilledema.

5. Posterior cerebral artery: paralysis of the third, fourth and sixth nerves. If the aneurysm develops in the brain substance, it is indistinguishable from a neoplasm in the same region, and homonymous hemianopsia or visual aphasia may be present.

It is evident that a paralysis of the third nerve is one of the most frequent symptoms (30 per cent of all cases in this series) and that it is particularly suggestive of an aneurysm of the internal carotid artery.

Ophthalmologists may be interested to learn that many aneurysms have a congenital origin and are due to the incomplete involution of temporary arteries. The primitive ophthalmic artery is one of the vessels which are responsible for such aneurysms.

An interesting chapter deals with the embryology and anatomy of the circle of Willis, and another is devoted to the surgical treatment. It is encouraging to know that in the last twenty years 64 aneurysms were treated surgically. In the last six and one-quarter years, 36 cases of aneurysm were observed, in 30 of these operation was performed, with cure in 21 cases and death in only 9 cases.

The book is evidently designed to be read by neurosurgeons, and the author has therefore dealt in detail with the operative procedures, but there is much which will interest the ophthalmologist. The print and illustrations are clear.

EDWARD HARTMANN



# Directory of Ophthalmologic Societies \*

## INTERNATIONAL

### INTERNATIONAL ASSOCIATION FOR PREVENTION OF BLINDNESS

President Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France

Secretary-General Prof M Van Duyse, Université de Gand, Gand, Prov Ostflandern, Belgium

All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6<sup>e</sup>, France

### INTERNATIONAL OPHTHALMOLOGIC CONGRESS

President Prof Nordenson, Serafimerlasarettet, Stockholm, Sweden

Secretary Dr Ehlers, Jerbanenegade 41, Copenhagen, Denmark

### INTERNATIONAL ORGANIZATION AGAINST TRACHOMA

President Dr A F MacCallan, 17 Horseferry Rd, London, England

### PAN-AMERICAN CONGRESS OF OPHTHALMOLOGY

President Dr Harry S Gradle, 58 E Washington St, Chicago

Executive Secretaries Dr Conrad Berens, 35 E 70th St, New York. Dr M E Alvaro, 1511 Rua Consolacão, São Paulo, Brazil

## FOREIGN

### ALL-INDIA OPHTHALMOLOGICAL SOCIETY

President Dr B K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore

Secretary Dr G Zachariah, Flitcham, Marshall's Rd, Madras

### BRITISH MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President Dr W. Clark Souter, 9 Albyn Pl, Aberdeen, Scotland

Secretary Dr Frederick Ridley, 12 Wimpole St, London, W 1

### CHENG TU OPHTHALMOLOGICAL SOCIETY

President Dr Eugene Chan

Secretary Dr K S Sun

Place Eye, Ear, Nose and Throat Hospital, Chengtu, China

### CHINESE OPHTHALMOLOGY SOCIETY

President Dr C H Chou, 363 Avenue Haig, Shanghai

Secretary Dr F. S Tsang, 221 Foochow Rd, Shanghai

### CHINESE OPHTHALMOLOGICAL SOCIETY OF PEIPING

President Dr H T Pi, Peiping Union Medical College, Peiping

Secretary Dr C K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping

Place Peiping Union Medical College, Peiping Time Last Friday of each month

### GERMAN OPHTHALMOLOGICAL SOCIETY

President Prof W Lohlein, Berlin

Secretary Prof E Engelking, Heidelberg

### HUNGARIAN OPHTHALMOLOGICAL SOCIETY

President Prof I Imre, Budapest

Assistant Secretary Dr Stephen de Grósz, University Eye Hospital, Mariautca 39, Budapest

All correspondence should be addressed to the Assistant Secretary

### MIDLAND OPHTHALMOLOGICAL SOCIETY

President Dr. W Niccol, 4 College Green, Gloucester, England.

Secretary Mr T Harrison Butler, 61 Newhall St, Birmingham 3, England

Place Birmingham and Midland Eye Hospital

### NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President Mr John Foster, 45 Park Sq, Leeds

Secretary Mr William M Muirhead, 70 Upper Hanover St, Sheffield

Place Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation Time October to April

### OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President Dr A James Flynn, 135 Macquarie St, Sydney

Secretary Dr D Williams, 193 Macquarie St, Sydney

### OPHTHALMOLOGICAL SOCIETY OF EGYPT

President Prof Dr Mohammed Mahfouz Bey, Government Hospital, Alexandria

Secretary Dr Mohammed Khalil, 4 Bachler St, Cairo

All correspondence should be addressed to the secretary, Dr Mohammed Khalil

### OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President Mr Charles B Goulden, OBE, MD, MCh, 89 Harley St, London

Secretary Mr Frank W Law, MA, MD, FRCS, 30 Devonshire Pl, London W 1

### OPHTHALMOLOGY SOCIETY OF BOMBAY

President Dr D D Sathaye, 127 Girgaum Rd, Bombay 4, India

Secretary Dr H D Dastur, Dadar, Bombay 14, India

Place H B A Free Ophthalmic Hospital, Parel, Bombay 12 Time First Friday of every month

### OXFORD OPHTHALMOLOGICAL CONGRESS

Master Mr. P G. Doyne, 60 Queen Anne St, London, W 1, England

Secretary-Treasurer Dr. F A Anderson, 12 St John's Hill, Shrewsbury, England

Place Oxford, England Time July 8-9, 1943

### PALESTINE OPHTHALMOLOGICAL SOCIETY

President Dr Arich Feigenbaum, Abyssinian St 15, Jerusalem

Secretary Dr E Sinai, Tel Aviv

### POLISH OPHTHALMOLOGICAL SOCIETY

President Dr W Kapuściński, 2 Waly Batorego, Poznań

Secretary Dr. J Sobański, Lindley'a 4, Warsaw

Place Lindley'a 4, Warsaw

### ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President Col F A Juler, 96 Harley St, London, W 1, England

Secretary Dr Harold Ridley, 60 Queen Anne St, London, W 1, England

\* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date

## SÃO PAULO SOCIETY OF OPHTHALMOLOGY

President Prof Moacyr E Alvaro, Consolação 1151, São Paulo, Brazil  
 Secretary Dr Silvio de Almeida Toledo, Enfermaria Santa Luzia, Santa Casa de Misericórdia, Cesario Motta, St 112, São Paulo, Brazil

## SCOTTISH OPHTHALMOLOGICAL CLUB

President Dr S Spence Meighan, 13 Woodside Pl, Glasgow, C 3  
 Secretary Dr Alexander Garrow, 15 Woodside Pl, Glasgow, C 3  
 Place Edinburgh and Glasgow, in rotation

## SOCIEDAD ARGENTINA DE OFTALMOLOGIA

Chairman Dr Jorge Malbran, Buenos Aires  
 Secretary Dr Benito Just Tiscornia, Santa Fe 1171, Buenos Aires

## SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President Prof Dr Carlos Weskamp, Laprida 1159, Rosario  
 Secretary Dr Juan M Vila Ortiz, Cordoba 1433, Rosario  
 Place Rosario Time Last Saturday of every month, April to November, inclusive All correspondence should be addressed to the President

## SOCIEDADE DE OFTALMOLOGIA DE MINAS GERAIS

President Prof Hilton Rocha, Rua Rio de Janeiro 2251, Bello Horizonte, Minas Geraes, Brazil  
 Secretary Dr Ennio Coscarelli, Rua Amores 1697, Bello Horizonte, Minas Geraes, Brazil

## SOCIEDADE DE OFTALMOLOGIA E OTORRINOLARINGOLOGIA DE RIO GRANDE DO SUL

President Dr Luiz Assumpção Osorio, Edifício Vera Cruz, Apartamento 134, Porto Alegre, Rio Grande do Sul  
 Secretary Dr Fernando Voges Alves, Caixa Postal 928, Porto Alegre, Rio Grande do Sul

## SOCIEDADE DE OPHTHALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President Dr Theonilo Amorim, Barra Avenida, Bahia, Brazil  
 Secretary Dr Adroaldo de Alencar, Brazil  
 All correspondence should be addressed to the President

## SOCIETÀ OFTALMOLOGICA ITALIANA

President Prof Dott Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome  
 Secretary Prof Dott Epimaco Leonardi, Via del Gianicolo, 1, Rome

## SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary Dr René Onfray, 6 Avenue de la Motte Picquet, Paris, 7<sup>e</sup>

## SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President Prof K G Ploman, Stockholm  
 Secretary Dr K. O Granstrom, Sodermalmstorg 4 III tr, Stockholm, So

## TEL AVIV OPHTHALMOLOGICAL SOCIETY

President Dr D Arich-Friedman, 96 Allenby St, Tel Aviv, Palestine.  
 Secretary Dr Sadger Max, 9 Bialik St, Tel Aviv, Palestine.

## NATIONAL

## AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman Dr Frederick C Cordes, 384 Post St, San Francisco  
 Secretary Dr R J Masters, 23 E Ohio St, Indianapolis  
 Place New York Time June 11-15, 1945

## AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President Dr Lawrence T Post, Metropolitan Bldg, St Louis  
 President-Elect Dr Gordon B New, Mayo Clinic, Rochester, Minn  
 Executive Secretary-Treasurer Dr William L Benedict, 101-1st Ave Bldg, Rochester, Minn

## AMERICAN OPHTHALMOLOGICAL SOCIETY

President Dr S Judd Beach, 704 Congress St, Portland, Maine  
 Secretary-Treasurer Dr Walter S Atkinson, 129 Clinton St, Watertown, N Y

## ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC

Chairman Dr Conrad Berens, 35 E 70th St, New York  
 Secretary-Treasurer Major Brittain F Payne, School of Aviation Medicine, Randolph Field, Texas  
 Assistant Secretary-Treasurer Dr Hunter Romaine, 35 E 70th St, New York

## CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President Dr Alexander E MacDonald, 170 St George St, Toronto  
 Secretary-Treasurer Dr L J Sebert, 170 St George St, Toronto

## CANADIAN OPHTHALMOLOGICAL SOCIETY

President Dr R Evatt Mathers, 34½ Morris St, Halifax, N S  
 Secretary-Treasurer Dr Kenneth B Johnston, Suite 1, 1509 Sherbrooke St W, Montreal

## NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President Mr Mason H Bigelow, 1790 Broadway, New York  
 Secretary Miss Regina E Schneider, 1790 Broadway, New York  
 Executive Director Mrs Eleanor Brown Merrill, 1790 Broadway, New York

## SECTIONAL

## ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President Dr N Zwaifler, 46 Wilbur Ave, Newark  
 Secretary Dr William F Keim Jr, 25 Roseville Ave, Newark  
 Place 91 Lincoln Park South, Newark Time 8 45 p m, second Monday of each month, October to May

## CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr L J Friend, 425 E Grand Ave, Beloit, Wis  
 Secretary Dr G L McCormick, 626 S Central Ave, Marshfield

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President Dr Paul A Chandler, 5 Bay State Rd, Boston  
 Secretary-Treasurer Dr Merrill J King, 264 Beacon St, Boston  
 Place Massachusetts Eye and Ear Infirmary, 243 Charles St, Boston Time 8 p m, third Tuesday of each month from November to April, inclusive

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President Dr D H O'Rourke, 1612 Tremont Pl, Denver  
 Secretary-Treasurer Dr C Allen Dickey, 450 Sutter St, San Francisco

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr L L Bull, 1215-14th Ave, Seattle, Wash  
 Secretary-Treasurer Dr Barton E Peden, 301 Stimson Bldg, Seattle 1  
 Place Seattle or Tacoma, Wash Time Third Tuesday of each month except June, July and August

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President Dr J Sheldon Clark, 27 E Stephenson St, Freeport, Ill  
 Secretary-Treasurer Dr Harry R Warner, 321 W State St, Rockford, Ill  
 Place Rockford, Ill, or Janesville or Beloit, Wis Time Third Tuesday of each month from October to April, inclusive

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr M H Pike, Midland, Mich  
 Secretary-Treasurer Dr H H Heuser, 207 Davidson Bldg, Bay City, Mich  
 Place Saginaw or Bay City, Mich Time Second Tuesday of each month, except July, August and September

SIoux VALLEY EYE AND EAR ACADEMY

President Dr J C Decker, 515 Francis Bldg, Sioux City, Iowa  
 Secretary-Treasurer Dr J E Dvorak, 408 Davidson Bldg, Sioux City, Iowa

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman Dr John H Burleson, 414 Navarro St, San Antonio, Texas  
 Secretary Dr J W Jervey Jr, 101 Church St, Greenville, S C

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President Dr H L Brehmer, 221 W Central Ave, Albuquerque, N Mex  
 Secretary Dr A E Cruthirds, 1011 Professional Bldg, Phoenix, Ariz

SOUTHWESTERN MICHIGAN TRILOGICAL SOCIETY

President Dr W M Dodge, 716 First National Bank Bldg, Battle Creek  
 Secretary-Treasurer Dr Kenneth Lowe, 25 W Michigan Ave, Battle Creek  
 Time Last Thursday of September, October, November, March, April and May

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Ray Parker, 218 Franklin St, Johnston, Pa  
 Secretary-Treasurer Dr J McClure Tyson, Deposit Nat'l Bank Bldg, DuBois

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President Dr Raymond C Cook, 701 Main St, Little Rock  
 Secretary Dr K W Cosgrove, Urquhart Bldg, Little Rock

COLORADO OPHTHALMOLOGICAL SOCIETY

President Dr C A Ringle, 912-9th Ave, Greeley  
 Secretary Dr W A Ohmart, 1102 Republic Bldg, Denver  
 Place University Club, Denver Time 7 30 p m, third Saturday of each month, October to May, inclusive

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President Dr F L Phillips, 405 Temple St, New Haven  
 Secretary-Treasurer Dr W H Turnley, 1 Atlantic St, Stamford, Conn

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President William O Martin Jr, Doctors Bldg, Atlanta  
 Secretary-Treasurer Dr C K McLaughlin, 526 Walton St, Macon

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr F McK Ruby, Union City  
 Secretary Dr Edwin W Dyar Jr, 23 E Ohio St, Indianapolis  
 Place French Lick Time First Wednesday in April

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr J K Von Lackum, 117-3d St S E, Cedar Rapids  
 Secretary-Treasurer Dr B M Merkel, 604 Locust St, Des Moines

KANSAS STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr W D Pittman, Pratt  
 Secretary Dr Louis R Haas, 902 N Broadway, Pittsburg

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr Val H Fuchs, 200 Carondelet St, New Orleans  
 Secretary-Treasurer Dr Edley H Jones, 1301 Washington St, Vicksburg, Miss

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr Robert H Fraser, 25 W Michigan Ave, Battle Creek  
 Secretary Dr R G Laird, 114 Fulton St, Grand Rapids

# MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr George E McGeary, 920 Medical Arts Bldg, Minneapolis  
 Secretary Dr William A Kennedy, 372 St. Peter St, St Paul  
 Time Second Friday of each month from October to May

# MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President Dr William Morrison, 208 N Broadway, Billings, Mont  
 Secretary Dr Fritz D Hurd, 309 Medical Arts Bldg, Great Falls

# NEBRASKA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha  
 Secretary-Treasurer Dr John Peterson, 1307 N St, Lincoln

# NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY, OTOTOLOGY AND RHINOLARYNGOLOGY

Chairman Dr B E Failing, 31 Lincoln Park, Newark  
 Secretary Dr George Meyer, 410 Haddon Ave, Camden

# NEW YORK STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

Chairman Dr Harold J Joy, 504 State Tower Bldg, Syracuse 2  
 Secretary Dr Maxwell D Ryan, 660 Madison Ave, New York 21

# NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Hugh C Wolfe, 102 N Elm St, Greensboro  
 Secretary Dr Vanderbilt F Couch, 104 W 4th St, Winston-Salem

# NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr W L Diven, City National Bank Bldg, Bismarck.  
 Secretary-Treasurer Dr A E Spear, 20 W Villard, Dickinson

# OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Paul Neely, 1020 S W Taylor St, Portland  
 Secretary-Treasurer Dr Lewis Jordon, 1020 S W Taylor St, Portland  
 Place Good Samaritan Hospital, Portland Time Third Tuesday of each month

# PENNSYLVANIA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Lewis T Buckman, 83 S Franklin St, Wilkes-Barre  
 Secretary Pro Tem Dr Paul C Craig, 232 N 5th St, Reading  
 Time Last week in April

# RHODE ISLAND OPHTHALMOLOGICAL AND OTOTOLOGICAL SOCIETY

Acting President Dr. N Darrell Harvey, 112 Waterman St., Providence.  
 Secretary-Treasurer Dr Linley C Happ, 124 Waterman St, Providence  
 Place Rhode Island Medical Society Library, Providence Time 8 30 p m, second Thursday in October, December, February and April

# SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr J L Sanders, 222 N Main St, Greenville.  
 Secretary Dr J H Stokes, 125 W Cheves St, Florence

# TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Wesley Wilkerson, 700 Church St, Nashville  
 Secretary-Treasurer Dr W D Stinson, 124 Physicians and Surgeons Bldg, Memphis

# TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President Dr F H Rosebrough, 603 Navarro St, San Antonio  
 Secretary Dr M K McCullough, 1717 Pacific Ave, Dallas

# UTAH OPHTHALMOLOGICAL SOCIETY

President Dr R B Maw, 699 E South Temple, Salt Lake City  
 Secretary-Treasurer Dr Charles Ruggeri Jr, 1120 Boston Bldg, Salt Lake City  
 Place University Club, Salt Lake City Time 7 00 p m, third Monday of each month

# VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President Dr Mortimer H Williams, 30½ Franklin Rd. S W, Roanoke  
 Secretary-Treasurer Dr Meade Edmunds, 34 Franklin St, Petersburg

# WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President Dr George Traugh, 309 Cleveland Ave, Fairmont  
 Secretary Dr Welch England, 621½ Market St, Parkersburg

# LOCAL

# AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr E L Mather, 39 S Main St, Akron, Ohio  
 Secretary-Treasurer Dr V C Malloy, 2d National Bank Bldg, Akron, Ohio  
 Time First Monday in January, March, May and November

# ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr B M Cline, 153 Peachtree St N E, Atlanta, Ga  
 Acting Secretary Dr A V Hallum, 478 Peachtree St. N E, Atlanta, Ga  
 Place Grady Hospital Time 6 00 p m, fourth Monday of each month, from October to May

BALTIMORE MEDICAL SOCIETY, SECTION ON  
OPHTHALMOLOGY

Chairman Dr Ernst Bodenheimer, 1212 Eutaw Pl,  
Baltimore  
Secretary Dr. Thomas R O'Rourke, 104 W. Madison  
St, Baltimore  
Place Medical and Chirurgical Faculty, 1211 Cathedral  
St. Time 8 30 p m, fourth Thursday of each  
month from October to March

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President. Each member, in alphabetical order  
Secretary Dr. Luther E Wilson, 919 Woodward Bldg,  
Birmingham, Ala  
Place Tutwiler Hotel Time 6 30 p m, second  
Tuesday of each month, September to May, inclusive

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President Dr Michael J Buonaguro, 589 Lorimer St,  
Brooklyn  
Secretary-Treasurer Dr Benjamin C Rosenthal, 140  
New York Ave, Brooklyn 16  
Place Kings County Medical Society Bldg, 1313 Bed-  
ford Ave Time Third Thursday in February, April,  
May, October and December.

BUFFALO OPHTHALMOLOGIC CLUB

President Dr Walter F King, 519 Delaware Ave,  
Buffalo  
Secretary-Treasurer Dr Sheldon B Freeman, 196  
Linwood Ave, Buffalo  
Time Second Thursday of each month

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Each member, in alphabetical order  
Secretary Dr Douglas Chamberlain, Chattanooga  
Bank Bldg, Chattanooga, Tenn  
Place Mountain City Club Time Second Thursday  
of each month from September to May

CHICAGO OPHTHALMOLOGICAL SOCIETY

President Dr Vernon M Leech, 55 E Washington  
St, Chicago  
Secretary Dr W A Mann, 30 N Michigan Ave,  
Chicago  
Place Chicago Towers Club, 505 N Michigan Ave  
Time Third Monday of each month from October  
to May

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY  
STAFF

Chairman Dr D T Vail, 441 Vine St, Cincinnati  
Secretary Dr A A Levin, 441 Vine St, Cincinnati  
Place Cincinnati General Hospital Time 7 45 p m,  
third Friday of each month except June, July and  
August

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman Dr Shandor Monson, 1621 Euclid Ave,  
Cleveland  
Secretary Dr Carl Ellenberger, 14805 Detroit Ave,  
Cleveland  
Time Second Tuesday in October, December, February  
and April.

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION  
ON OPHTHALMOLOGY

Chairman Dr W S. Reese, 1901 Walnut St,  
Philadelphia  
Clerk Dr George F J Kelly, 37 S 20th St,  
Philadelphia  
Time Third Thursday of every month from October  
to April, inclusive

COLUMBUS OPHTHALMOLOGICAL AND OTO-  
LARYNGOLOGICAL SOCIETY

Chairman Dr. H. D Emswiler, 370 E Town St,  
Columbus, Ohio  
Secretary-Treasurer Dr D G Sanor, 206 E State  
St, Columbus, Ohio  
Place The Neil House Time 6 p m, first Monday  
of each month

CORPUS CHRISTI EYE, EAR, NOSE AND  
THROAT SOCIETY

Chairman Dr Arthur Padillo, 414 Medical Profes-  
sional Bldg, Corpus Christi, Texas  
Secretary Dr Edgar G Mathis, 815 Medical Arts  
Bldg, Corpus Christi, Texas  
Time Second Friday of each month from October to  
May

DALLAS ACADEMY OF OPHTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr Ruby K Daniel, Medical Arts Bldg,  
Dallas 1, Texas  
Secretary Dr Tom Barr, Medical Arts Bldg, Dallas 1,  
Texas  
Place Dallas Athletic Club Time 6 30 p m, first  
Tuesday of each month from October to June The  
November, January and March meetings are devoted  
to clinical work

DES MOINES ACADEMY OF OPHTHALMOLOGY AND  
OTOLARYNGOLOGY

President Dr H C Schmitz, 604 Locust St, Des  
Moines, Iowa  
Secretary-Treasurer Dr Byron M Merkel, 604 Locust  
St, Des Moines, Iowa  
Time 7 45 p m, third Monday of every month from  
September to May

DETROIT OPHTHALMOLOGICAL CLUB

Chairman Members rotate alphabetically  
Secretary Dr Cecil W Lepard, 1025 David Whitney  
Bldg, Detroit  
Place Club rooms of Wayne County Medical Society  
Time First Wednesday of each month, November  
through April

DETROIT OPHTHALMOLOGICAL SOCIETY

President Dr Parker Heath, 1553 Woodward Ave,  
Detroit  
Secretary Dr Leland F Carter, 1553 Woodward Ave,  
Detroit  
Place Club rooms of Wayne County Medical Society  
Time Third Thursday of each month from Novem-  
ber to April, inclusive

EASTERN NEW YORK EYE, EAR, NOSE AND  
THROAT ASSOCIATION

President Appointed at each meeting  
Secretary-Treasurer Dr Joseph L Holohan, 330 State  
St, Albany  
Time Third Wednesday in October, November, March,  
April, May and June

## FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Rex Howard, 602 W 10th St., Fort Worth, Texas  
 Secretary-Treasurer Dr R H Gough, Medical Arts Bldg, Fort Worth, Texas  
 Place Medical Hall, Medical Arts Bldg Time 7 30 p m, first Friday of each month except July and August

## HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SECTION

President Dr Lyle J Logue, 1304 Walker Ave., Houston, Texas  
 Secretary Dr John T Stough, 803 Medical Arts Bldg, Houston, Texas  
 Place Medical Arts Bldg, Harris County Medical Society Rooms Time 8 p m, second Thursday of each month from September to June

## INDIANAPOLIS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President Dr Myron Harding, 23 E Ohio St, Indianapolis  
 Secretary Dr Kenneth L Craft, 23 E Ohio St, Indianapolis  
 Place Indianapolis Athletic Club Time 6 30 p m, second Thursday of each month from November to May

## KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Edgar Johnson, 906 Grand Ave, Kansas City, Mo  
 Secretary Dr W E Keith, 1103 Grand Ave, Kansas City, Mo  
 Time Third Thursday of each month from October to June The November, January and March meetings are devoted to clinical work

## LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr Harold Snow, 614 S Pacific Ave, San Pedro, Calif  
 Secretary-Treasurer Dr Oliver R Nees, 508 Times Bldg, Long Beach, Calif  
 Place Professional Bldg Time Last Wednesday of each month from October to May

## LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr M E Trainor, 523 W 6th St, Los Angeles  
 Secretary-Treasurer Dr Orrie E Ghrist, 210 N Central Ave, Glendale, Calif  
 Place Los Angeles County Medical Association Bldg, 1925 Wilshire Blvd Time 6 00 p m, fourth Monday of each month from September to May, inclusive

## LOUISVILLE EYE AND EAR SOCIETY

President Dr Joseph S Heitger, Heyburn Bldg, Louisville, Ky  
 Secretary-Treasurer Dr J W Fish, 321 W Broadway, Louisville, Ky  
 Place Brown Hotel Time 6 30 p m, second Thursday of each month from September to May, inclusive

## LOWER ANTHRACITE EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Each member in alphabetical order  
 Secretary Dr James J Monohan, 31 S Jardin St, Shenandoah, Pa

## MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr P S Constantinople, 1835 I St N W, Washington  
 Secretary Dr Frazier Williams, 1801 I St N W Washington  
 Place 1718 M St N W Time 8 p m, third Friday of each month from October to April, inclusive

## MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Each member in alphabetical order  
 Secretary Dr Sam H Sanders, 1089 Madison Ave, Memphis, Tenn  
 Place Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital Time 8 p m, second Tuesday of each month from September to May

## MILWAUKEE OTO-OPHTHALMIC SOCIETY

President Dr Edwin C Bach, 324 E Wisconsin Ave, Milwaukee  
 Secretary-Treasurer Dr Ralph T Rank, 238 W Wisconsin Ave, Milwaukee  
 Place University Club Time 6 30 p m, second Tuesday of each month

## MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman Dr H V Dutrow, 1040 Fidelity Medical Bldg, Dayton, Ohio  
 Secretary-Treasurer Dr Maitland D Place, 981 Reibold Bldg, Dayton, Ohio  
 Place Van Cleve Hotel Time 6 30 p m, first Tuesday of each month from October to June, inclusive

## MONTREAL OPHTHALMOLOGICAL SOCIETY

President Dr J Rosenbaum, 1396 Ste Catherine St W, Montreal, Canada  
 Secretary Dr L Tessier, 1230 St Joseph Blvd E, Montreal, Canada  
 Time Second Thursday of October, December, February and April

## NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr M M Cullom, 700 Church St, Nashville, Tenn  
 Secretary Dr R E Sullivan, 432 Doctors Bldg, Nashville, Tenn  
 Place St. Thomas Hospital Time 8 p m, third Monday of each month from October to May

## NEW HAVEN OPHTHALMOLOGICAL SOCIETY

President Dr William H Ryder, 185 Church St, New Haven, Conn  
 Secretary Dr Frederick A Wiess, 255 Bradley St, New Haven, Conn

NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr W B Clark, 1012 American Bank Bldg, New Orleans  
 Secretary Dr Mercer G Lynch, 1018 Maison Blanche Bldg, New Orleans  
 Place Louisiana State University Medical Bldg  
 Time 8 p m, second Tuesday of each month from October to May

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman Dr Thomas H Johnson, 30 W 59th St, New York  
 Secretary Dr Wendell L Hughes, 131 Fulton Ave, Hempstead, N Y  
 Time 8 30 p m, third Monday of every month from October to May, inclusive

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President Dr Milton Berliner, 57 W 57th St, New York  
 Secretary Dr Benjamin Esterman, 983 Park Ave, New York  
 Place Squibb Hall, 745-5th Ave Time 8 p m, first Monday of each month from October to May, inclusive

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr James P Luton, 117 N Broadway, Oklahoma City  
 Secretary Dr Harvey O Randel, 117 N Broadway, Oklahoma City  
 Place University Hospital Time Second Tuesday of each month from September to May

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr D D Stonecypher, Nebraska City, Neb  
 Secretary-Treasurer Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha  
 Place Omaha Club, 20th and Douglas Sts, Omaha  
 Time 6 p m dinner, 7 p m program, third Wednesday of each month from October to May

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President Dr Thomas Sanfacon, 340 Park Ave, Paterson, N J  
 Secretary-Treasurer Dr J Averbach, 435 Clinton Ave, Clinton, N J  
 Place Paterson Eye and Ear Infirmary Time 9 p m, last Friday of every month, except June, July and August

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

President Dr Isaac Tassman, 136 S 16th St, Philadelphia  
 Secretary Dr Glen Gregory Gibson, 255 S 17th St, Philadelphia  
 Time First Thursday of each month from October to May

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President Dr George H Shuman, 351-5th Ave, Pittsburgh  
 Secretary Dr Robert J Billings, 509 Liberty Ave, Pittsburgh  
 Place Pittsburgh Academy of Medicine Bldg Time Fourth Monday of each month, except June, July, August and September

READING EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Michael J Ponta, 312 N 5th St, Reading, Pa  
 Secretary Dr Paul C Craig, 232 N 5th St, Reading, Pa  
 Place Wyomissing Club Time 6 30 p m, third Wednesday of each month from September to July

RICHMOND OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr Peter N Pastore, Medical College of Virginia, Richmond, Va  
 Secretary Dr Clifford A Folkes, Professional Bldg, Richmond, Va  
 Place Westmoreland Club Time 6 p m, second Monday of each month from October to May

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Frank Barber, 75 S Fitzhugh St, Rochester, N Y  
 Secretary-Treasurer Dr Charles T Sullivan, 277 Alexander St, Rochester, N Y

ST LOUIS OPHTHALMIC SOCIETY

President Dr C C Beisbarth, 3720 Washington Blvd, St Louis  
 Secretary Dr H R Hildreth, 508 N Grand Blvd, St Louis  
 Place Oscar Johnson Institute Time Clinical meeting, 5 30 p m, dinner and scientific meeting 6 30 p m, fourth Friday of each month from October to April, inclusive, except December

SAN ANTONIO OPHTHALMO-OTO-LARYNGOLOGICAL SOCIETY

President Dr Belvin Pritchett, 705 E Houston St, San Antonio 5, Texas  
 Secretary-Treasurer Lt Col John L Matthews, AAF School of Aviation Medicine, Randolph Field, Texas  
 Place San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center  
 Time 7 p m, second Tuesday of each month from October to May

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman Dr Roy H Parkinson, 870 Market St, San Francisco  
 Secretary Dr A G Rawlins, 384 Post St, San Francisco  
 Place Society's Bldg, 2180 Washington St, San Francisco Time Fourth Tuesday of every month except June, July and December

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President Dr David C Swearingen, Slattery Bldg, Shreveport, La  
 Secretary-Treasurer Dr Kenneth Jones, Medical Arts Bldg, Shreveport, La  
 Place Shreveport Charity Hospital Time 7 30 p m, first Monday of every month except July, August and September



SPOKANE ACADEMY OF OPHTHALMOLOGY AND  
OTO-LARYNGOLOGY

President Dr Clarence A Veasey Sr, 421 W River-  
side Ave, Spokane, Wash  
Secretary Dr Clarence A Veasey Jr, 421 W River-  
side Ave, Spokane, Wash  
Place Spokane Medical Library Time 8 p m, fourth  
Tuesday of each month except June, July and August

SYRACUSE EYE, EAR, NOSE AND  
THROAT SOCIETY

President Dr A H Rubenstein, 713 E Genesee St,  
Syracuse, N Y  
Secretary-Treasurer Dr I H Blaisdell, 713 E  
Genesee St, Syracuse, N Y  
Place University Club Time First Tuesday of each  
month except June, July and August

TOLEDO EYE, EAR, NOSE AND  
THROAT SOCIETY

Chairman Dr E W Campbell, 316 Michigan St,  
Toledo, Ohio  
Secretary Dr L C Ravin, 316 Michigan St, Toledo,  
Ohio  
Place Toledo Club Time Each month except June,  
July and August

TORONTO ACADEMY OF MEDICINE, SECTION OF  
OPHTHALMOLOGY

Chairman Dr W R F Luke, 316 Medical Arts Bldg,  
Toronto, Canada  
Secretary Dr W T Gratton, 216 Medical Arts Bldg,  
Toronto, Canada  
Place Academy of Medicine, 13 Queens Park Time  
First Monday of each month, November to April

WASHINGTON, D C, OPHTHALMOLOGICAL SOCIETY

President Dr S Bockoven, 1752 Massachusetts Ave,  
Washington, D C  
Secretary-Treasurer Dr John Lloyd, 1218-16th St  
N W, Washington, D C  
Place Medical Society of District of Columbia Bldg,  
1718 M St N W, Washington, D C Time 7 30  
p m, first Monday in November, January, March  
and May

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman Each member in turn  
Secretary Dr Samuel T Buckman, 70 S Franklin  
St, Wilkes-Barre, Pa  
Place Office of chairman. Time Last Tuesday of  
each month from October to May

